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# ASTHMA

## PRESENTING AN EXPOSITION
## OF
## THE NONPASSIVE EXPIRATION THEORY

BY

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TO MY WIFE
AND
TO MY MOTHER

THIS VOLUME IS MOST
AFFECTIONATELY DEDICATED

# PREFACE.

This monograph is the result of nine years' study of asthma. It is argumentative, supporting the "Nonpassive Expiration Theory" which is the culmination of my work to date.

The strongest features of the theory are that preasthmatic states can be recognized thereby and successfully combated, and that treatment of asthma can be removed from the field of empiricism and put upon a rational and scientific foundation.

Italics are used throughout the book to give evidence of the contents of paragraphs. In certain places, notably in Chapter III, the italics come within quotation marks, and are used irrespective of their existence in the original manuscript. In Chapter III italics show also what has previously been done in line with my work.

I am indebted to many of my friends for assistance—more especially to Drs. George Dock, John C. Morfit, Major G. Seelig, Daniel M. Shoemaker, Philip Skrainka, Reverend John C. Burke, Mr. Bliss Isely, and others for criticising manuscript; to Mr. Paul Berdanier for illustrations; to Drs. Augustus G. Pohlman, W. M. C. Bryan, Dennis E. Jackson, and others for valuable suggestions; to Misses Helen Tiesler, Ella Lawrence, and Harriet Eby for efficient library services.

ORVILLE HARRY BROWN.

Phoenix, Arizona.

# FOREWORD.

With the great range of special investigation in all departments of medicine, and the effort to explain all obscure features by applying new discoveries in every field of science, comes the need of making broad surveys—of gathering in a connected form the present status of various clinical problems.

The conditions included in the term "asthma" might well excite efforts at general study, and Dr. O. H. Brown has earned the gratitude of the profession by presenting a comprehensive and up-to-date study of them. The writer has had the privilege of following Dr. Brown's research over some years and of reading his manuscript, and has been impressed by the accuracy of the author's clinical work, and by the fullness and symmetry of the literary production. The literature, both monographic and special, is well presented, the theories of the disease are clearly set forth and critically discussed. The author's theory of asthma, named by him the "Nonpassive Expiration Theory," is stated clearly and in an admirable spirit. It would be superfluous to give an analysis of this theory here, since the chapter well repays careful study, and bears directly on the author's method of treatment, which is clearly presented and reveals the well-informed, accurate, and conscientious therapeutist. The student and the practitioner can find in this book a true picture of the previous speculations and present knowledge of asthma expressed clearly and concisely, a trustworthy guide in the examination and treatment of actual patients, and many suggestions for fresh explorations by the bedside and in the laboratory.

GEORGE DOCK.

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# ASTHMA

## CHAPTER I.

### INTRODUCTION.

Asthma, "dramatic in symptoms," "elusive in pathology," "cloaked in mystery," sometimes termed the "epilepsy of the lungs," has been the theme of much careful research and the subject of countless papers and discussions. Despite the fact that in more than 2000 years of study innumerable data on this malady have been acquired, asthmatics suffer now just as they always have. Were my pen facile enough to induce those who read this paragraph to read on from cover to cover, I believe much might be accomplished for the poor suffering asthmatics.

As a basis for my theory, which I have called "The Nonpassive Expiration Theory," it is necessary to have in mind the anatomy and physiology of the bronchi, lungs, and heart. The essential facts of the anatomy are: (1) the larger bronchi are firm-walled; (2) the small bronchioles have very thin walls; (3) the lobule is a wide expanse leading from the bronchiole with many ramifications of respiratory bronchioles, atria, infundibula, and alveoli; (4) the bronchial vein courses along the bronchi, giving many minute branches to the mucosa of the bronchi; and (5) the right coronary artery, nourishing the right side of the heart, arises from the aorta.

In regard to the facts of the physiology, I call special attention to the physics of the circulation and the manner in which respiration affects it, noting (1) that blood and lymph obey the movements of the chest just as does air; i. e., the fluid within the vessels contiguous to those of the chest will flow into the vessels within the chest during inspiration and will be hindered, stopped, or actually caused to flow backward during expiration; (2) under normal conditions inspiration is muscular and expiration passive; (3) forceful active expirations are prominent in coughing, sneezing, dyspnea, etc.; (4) such expirations will interfere with the flow of the blood into the chest in proportion to their force and suddenness; (5) the interference with the flow of the blood is due to the fact that the intrapulmonic pressure is greater than atmospheric during expiration; (6) the increased pressure is induced primarily within the alveoli, infundibula, atria, etc., because of the "muffler"-like construction of the lobules; (7) the tension within the firm-walled bronchi varies relatively little from the atmospheric during either phase of respiration; (8) therefore, during forceful expirations there is a tendency for the vessels of the bronchial mucosa to become greatly overfilled and distended, narrowing the lumen to such a grade perhaps as to interfere seriously with the exit of air; and (9) the right heart, during long periods of forceful expirations because of the heightened pulmonic artery blood pressure thereby engendered and because of a lack of an automatic increase in nourishment during these periods of greater stress, may suffer serious strain and thereby contribute materially to the damming of the blood and lymph to the large veins and immediate tributaries. A consideration of these facts should lead us to an understanding of the true nature of asthma.

I have wished to show also that of all the possible theories to explain dyspnea, there is but one—the nonpassive expiration theory—which can account for asthma.

Commonly nonpassive expiration is indirectly caused by respiratory tract catarrh; and this involving the bronchi, inflames and swells the bronchial mucosa, causing it to narrow the lumen of the bronchi, and thus induces simple dyspnea. Labored breathing causes force to be put on expiration, and thereby becomes potential asthma. Inflammation may extend to the bronchial mucosa from a nasal catarrh, an anaphylactic reaction, a sinusitis, a pyorrhea, a tonsillitis, or other foci of infection in the respiratory tract, or possibly from elsewhere about the body. The bronchial mucosa may be prepared by a chronic fibroid phthisis for the reception of pyogenic bacteria. In those instances where the tuberculous process is not so active as to kill within a few years, and yet is sufficiently active to keep up a constant irritation of the bronchial mucosa, good soil is created for other bacteria—commonly those of "colds," "grip," and other acute infections. Tuberculosis then may play an important role in the etiology of asthma.

The symptoms which are ordinarily observed in asthma are the result of the nonpassive expiration, of the factors which lead thereto, or of the conditions which result therefrom. As there are many and variable contributing causes of the forceful expirations, the symptoms may show wide variations in different cases. The first case which I attended—the one which led to this "Arbeit"—had terrible paroxysms of coughing preceding each attack of asthma; his face became purplish in color and swollen, and his neck veins greatly dilated during the spells; morphin and strychnin, in combination only, relieved him. From these observations my prejudice for the muscle spasm theory was dispelled, partially at least, and in place was implanted a conviction that in this case some serious disturbance in circulation resulted during the paroxysms of asthma. Since making the first observations I have become convinced through study of a large number of cases that all asthmatics display marked manifestations of circulatory change. I shall show later why these arise and also why many apparently divergent symptoms and conditions are related in cause or effect.

Proof of my theory is to be found (1) in the study of the anatomy and physiology of the bronchi, lungs, and heart; (2) in a careful study of asthmatics, considering especially the development of the paroxysms—more especially the first effect of the attacks on the individual's circulatory apparatus, the characteristics of the sputum, etc.; (3) in experiments which have been performed and which prove that normal individuals can produce in themselves signs of asthma by practicing nonpassive expiration, especially if "colds" exist; (4) in the marked swelling of the mucosa during the attacks and the narrowing of the lumen during expirations, which have been repeatedly seen and reported; (5) in the simultaneous disappearance of the mucosa swelling and the asthma following injections of adrenalin; (6) in the knowledge we have of the pathology of the disease, which indicates right heart strain, emphysema, and chronic bronchitis; (7) in the histories of the cases which I have studied, showing the great part played in all cases by coughing, sneezing, dyspnea, and respiratory tract catarrh; (8) in the clinical histories found in the literature, which sustain my own observations; (9) in the location and character of the râles, their decrease by deep quick inspirations, and their increase by forceful prolonged expirations; (10) in the results of treatment based upon the nonpassive expiration theory, which prove the importance of regulating the respiration and of curing the bronchitis and all foci of infections which tend to promote coughing, sneezing, dyspnea, and respiratory tract catarrh.

Emphysema is an important factor in asthma, developing from the same cause, and becoming permanent if the strength of the alveolar tissues has been insufficient to stand the strain of the nonpassive expiration.

Spasm of the bronchiolar muscle may be the cause of simple dyspnea, which in turn may lead to asthma; but it can at best, I think, be only one of many important contributing causes of asthma.

Nasal obstruction, polyps, asthmogenic foci, reflexes, etc., are of great importance in many cases because they produce bronchitis as well as abnormal breathing, and should be looked for in every case, and when found, given appropriate treatment. The same may be said of pyorrhea, tonsillitis, appendicitis, salpingitis, urethritis, vaginitis, etc.

There is unmistakable evidence of a connection in some instances between asthma and anaphylaxis. While an occasional enthusiast over anaphylaxis, as an explanation for most heretofore mysterious conditions, would explain all asthma on that basis, I shall show where this is but one of the many causes—unless all inflammation is considered anaphylactic in nature.

The diagnosis of asthma is ordinarily not difficult. But there has been a confusion in the use of the term, and also a tendency not to consider a condition with perhaps typically asthmatic characteristics as asthma, unless there be no easily demonstrable cause of the dyspnea. To illustrate: A man with all the signs of asthma, but with a large aortic aneurysm would be considered by some not to have "true" asthma. This "apparent," or "pseudo," asthma is explained by the theory herein advanced. The real difficulty in diagnosis is to discover all the factors tending to the continuation of the bronchitis, coughing, sneezing, dyspnea, etc.

Treatment, I think, becomes entirely rational even though frequently difficult and complex, in the light of the nonpassive expiration theory. Respiratory drill is applicable in all cases. But as the indirect causes are so variable, every case is a law unto itself in regard to the further treatment. After the complete diagnosis is made, the question is: What can be done for each of the conditions found? Perhaps the asthma will be relieved when treatment is given for syphilis or tuberculosis or bronchitis, or for sinusitis or nasal polyps, or for an eczema or a gall-bladder disease, or for tonsillitis, or a pyorrhea, etc. Strange cures result. The explanation for most of them will be found in the theory which I shall advance.

Prophylactic measures against asthma become evident and will be of the greatest efficacy. Coughing, sneezing, dyspnea, etc., and all causes leading thereto must be controlled. It may not be possible to prevent "colds," but the excessive coughing, sneezing, and other nonpassive expiration can be controlled.

Many things still need to be known before the asthma problem is settled. Among the many questions are: What are "colds?" How can they be prevented? How shall one recognize the preactive stage of tuberculosis? Is syphilis a marked contributing factor? How widespread is this disease? How will morals be improved? Do we drink too much alcohol and not enough water? Can living and working conditions be improved?

The immediately important problem, however, relates to the prevention of "colds," coughs, nonpassive expiration, teaching asthmatics how to breathe, and getting these facts into the possession of physicians.

# CHAPTER II.

## DEFINITION OF ASTHMA.

The word "asthma" is derived from the Greek word ξοθμα which means "panting." Dyspnea comes from two Greek words, δυσ and κνοη, the former meaning ill or hard, while the latter means breathing. Thus asthma is panting, and dyspnea is hard breathing; the two are synonymous so far as derivation goes.

Usage, however, has applied the word "asthma" to a definite type of dyspnea. Hence asthma becomes a qualifying word to dyspnea and the terms "asthma" and "asthmatic dyspnea" are synonymous.

The definitions of asthma found in the textbooks, while referring to one affection, are considerably at variance, for the reason that writers are prone to inject into definitions the essentials of pet theories as to the cause or pathology of the malady. Hence, since there are many theories, there are many definitions, and much confusion prevails.

Bree,[1] in 1811, speaking of the earlier writers on asthma, says: "They have involved us in the uncertainty of their own conjectures. If we are to believe them, the nerves have been implanted in the animal system to remind man of his misfortunes and to betray the economy of life into perpetual derangement and torments scarcely to be endured." This quotation certainly does not apply as aptly to the writers since Bree's time as he thought it applied to those before him.

In 1908 the Editor of the Department of Therapeutics of the *Journal of the American Medical Association*,[2] after stating that asthma may be due to nasal abnormalities, bronchitis, hay fever, dust, drug irritants, etc., says, "Asthma, however, is frequently a neurosis alone, not being caused by any one particular condition or irritation. This is pure 'cussed' asthma and has been termed 'epilepsy of the lungs.'" The author holds that the essential cause is likely some condition of the blood. From *Progressive Medicine*,[3] I quote: "The truth about asthma is that it is an antiphysiological unruliness, occurring in function which is viscero-voluntary. The sympathetic and cerebrospinal systems go shares in the mutiny."

Gibson,[4] writing in the *British Medical Journal* in 1911, refers to the lack of understanding of asthma, and I quote from him as follows: "Its dramatic symptoms, its elusive pathology, its uncertain therapeutics may well be said to invest the subject of asthma with a cloud of mystery." Spicer,[5] in speaking of the word "asthma," says it is used sometimes "in a highly restricted sense for pure spasmodic or nerve asthma—'original sin' or 'depravity' of the respiratory center" without any initial peripheral irritation in existence or with only an unrecognized one.

That so much confusion has consistently endured is due, I think, to the fact that physicians ordinarily have poor opportunities to study asthma. A physician is usually called after the attack is developed and he remains with the patient long enough to give some relief and perhaps to hear the relatives' ideas of the paroxysms; he may prescribe medicine to be taken in the interim between attacks, but as a rule he does not see the patient again until another paroxysm develops. Quoting from Kidd,[6] "Asthmatics are generally so well up on their own cases that it is very rarely physicians have opportunities of seeing them during the fits." I emphasize, rarely does the physician see an attack begin, reach a climax, and subside unless he himself is the victim—in which case he is a biased, inefficient observer. Salter[7] has a physician-patient say, "In one's own personal case, one is prone to omit or slur over important facts just because of one's perfect familiarity with them."

The term "asthma" is used, however, to apply specifically to that type of dyspnea characterized by (1) prolonged and difficult expiration, especially if the attack be well developed (in the beginning of a paroxysm, however, both inspiration and expiration may appear equally difficult); (2) a marked distention—emphysema—of the chest; (3) wheezing and sonorous sounds with both phases of respiration, but especially with expiration; (4) signs of circulatory disturbance—cyanosis and distention of the neck and face blood vessels; (5) secretory changes in the bronchial mucosa, usually producing a considerable quantity of mucus, casts, plugs, crystals, etc.; and (6) a standing or sitting posture with arms and shoulders braced so as to bring the muscles of expiration into best use.

Labored breathing, unaccompanied by difficult expiration, noises within the bronchi, and chest distention is not asthma; it is simply dyspnea, but may be the precursor of asthma.

There has been some discussion as to whether asthma should be considered a disease—a distinct entity—or a symptom of any one of a number of diseases. I believe such argument is a waste of good breath. As will be seen by reading the subsequent chapters, the opinion will be expressed that asthma develops secondarily to bronchitis, tuberculosis, nasal disease, etc., and in this connection is properly considered merely a symptom. But theoretically at least, asthma may originate independently of an inflammatory state of the bronchial mucosa, and, in fact, with no pathologic change save that of forced expiration. Therefore, in this respect asthma may properly be considered a disease. If nephritis, endocarditis, etc., are diseases rather than symptoms, then asthma is a disease. The former have definite changes in structure as well as in function; the latter also has both, but the structural changes may be temporary and even when permanent, may not be marked and wholly peculiar to this condition; but nevertheless they are not to be denied.

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# CHAPTER III.

## HISTORICAL OBSERVATIONS AND THEORIES.

The historical data herein presented are as far as possible arranged chronologically. I offer no apology for presenting an extensive bibliography, even though the greater number of the findings and opinions are of comparatively little benefit in helping me to arrive at my conclusions. The names of physicians of rank of the past are all too infrequently seen in modern medical literature. If this historical sketch of asthma serves to quicken the interest of even a few in the subject of medical history, some good will have been accomplished.

A survey of the literature reveals that asthma has been recognized for centuries, even from the time of Hippocrates. Probably, however, there has been, and not very remotely, much confusion of other conditions with asthma, but perhaps not more than is the case with other poorly understood subjects.

The disease was first considered to be due to a spasm of the lungs. Then later it was suggested that there might be muscle in the bronchi and that these might undergo spastic contraction. This theory held sway from the seventeenth century even to the present. In the latter part of the nineteenth century the theory of vessel turgescence of the bronchial mucosa developed and divided honors with the muscle spasm theory. During the past decade the theory of anaphylaxis has become popular and has given further support to the muscle spasm theory. But a great proportion of physicians have not been satisfied with either of the two generally accepted theories. The multitude of theories, some ingenious and helpful and others far fetched and convincing evidence of a fruitless search, have failed to receive much attention. Incidentally many interesting but disconnected facts have been presented.

Hippocrates[1] referred frequently to asthma, saying, "Those who have passed their youth are subject to asthma, pleurisies, and inflammations of the lungs."

Aretaeus[2] describes asthmatics as follows: "*They breathe standing* as if desiring to draw in all the air which they possibly can inhale; and in their want of air they also open the mouth as if thus to enjoy the more of it; pale of countenance except the *cheeks* which *are ruddy;* sweat about the forehead and clavicles; *cough incessant and laborious;* expectoration small, thin, cold, resembling the efflorescence of foam; *neck swells* with the inflation of the breath (pneuma); the precordia retracted; pulse small, dense, compressed; legs slender; and if these symptoms increase, they *sometimes produce suffocation* after the form of epilepsy.

"But if it takes a favorable turn, *cough more protracted* and rarer; a more copious expectoration of more fluid matters; discharges from the bowels plentiful and watery; secretion of urine copious, although unattended with sediment; voice louder; sleep sufficient; relaxation of the precordia; sometimes a pain comes into the back during the remission; panting rare, soft, hoarse. Thus they escape a fatal termination. But during the remissions, although they may walk about erect, they bear traces of the affection."

Celsus[3] regarded dyspnea, orthopnea, and asthma as only modifications of the same malady differing from each other in degree. Wood makes Celsus say: "Each consists in difficulty of breathing. When this difficulty is more moderate and unsuffocative, it is called dyspnea; when it is more vehement so that the *breathing is sonorous and wheezing,* it constitutes asthma; and when it can only take place in an erect position, it is denominated orthopnea. The first is usually a chronic affection, the latter two, acute."

Galen[4] makes two causes only of asthma. Each is distinguished by a material producing irritation; i. e., *thick and pituitous humors and a crude tubercle in the lungs.*

Paulus Ægineta[5] says: "Those who breathe thick without fever, like those who have run fast, are said to be asthmatic, that is to say, to pant for breath; and from their being obliged to keep the chest erect for fear of being suffocated they are called orthopneic. The *affection arises from thick and viscid humors* becoming infarcted in the bronchial cells of the lungs. Dyspnea is a common symptom which accompanies these and many other complaints. The indication of cure in asthmatic complaints is to consume the viscid and thick humor by attenuant and retergent medicines."

Van Helmont[6] had a theory that "Archeus"—a something—a vital spirit—was enshrined in the stomach, and when disturbed, was responsible for disease by sending forth a peculiar fluid, which, reaching the lungs, caused asthma.

It seems to have remained for Willis[7] to describe the convulsive character of the respiration in asthmatic attacks. He held that the cause was some humor in the blood, and classified asthma under two heads; namely, pneumonic asthma, where *the essential process* was *a stopping up of the bronchial tubes;* and convulsive asthma, where there was a cramp of the muscles.

Following Willis, came Hoffmann,[8] Morgagni,[9] Floyer,[10] and others. Floyer offered the suggestion that asthma might be the result of *herpetic eruptions occurring on the bronchial mucosa* instead of on the skin. Morgagni criticized the views of Willis and added that it *seemed* to him *that concretions in the bronchial tubes were responsible for asthma.* He *found extravasated serum in the vesicles of the lungs in most cases.*

Haller[11] expressed the view that the *normal act of expiration hindered the flow of blood through the lungs.* He demonstrated that the lung contracted when concentrated acid was applied to it. Heberden,[12] under the heading "convulsive asthma," described what is now recognized as angina pectoris. Varnier[13] found that irritating liquids or fumes forced into the lungs caused contraction thereof.

Vogel,[14] Quarin,[15] and others further complicated the problems connected with asthma by classifying angina pectoris and such like conditions under the heading of asthma. Cullen[16] was probably the first to suggest that asthma might be the result of spasm of muscles of the finer bronchi. Thilenius[17] agreed with those who thought angina pectoris was a type of asthma. Truka[18] believed that herpetic, rheumatic, gouty, or hemorrhoidic affections were transmuted into asthma. Goodwin[19] poured water into the lungs of a cat through an opening in the trachea and found that the animal developed a great difficulty of respiration.

In 1811, Bree[20] who was a sufferer from asthma, published the fourth edition of his book on the subject, including in it the more important views which had been expressed on the disease up to that time. His theory of the cause—and it attracted much attention at the time—held the disease to be "an excessive contraction of all the muscles of respiration without acute fever, excited by an irritant in some of the viscera whose functions these muscles are intended to serve."

He compares the spasms of the asthmatic attacks to the tenesmus and griping dysentery; in both the effort is to get rid of the irritating material. Bree performed Goodwin's experiment of pouring water into the lungs of a dog and felt that he produced a type of breathing in the dog which closely simulated the asthmatic dyspnea of the human. Rostand[21] said that he *always found* in the numerous cases which had come under his notice, a *sufficiency of pathological changes to account for the dyspnea,* and saw no reason to assign this to a derangement of the nervous system. He admits the possibility, however, that a contraction of the muscle fibers of the bronchi might result independently of other pathology. This he designated as an idiopathic or nervous convulsive asthma.

Wedemeyer[22] demonstrated that mechanical or galvanic stimulation of the larger bronchi did not produce a narrowing of the lumen, whereas the stimulus, if applied to those of 0.5 to 1.0 mm. in diameter, produced a positive narrowing of their lumen. Louis[23] *believed the dyspnea of asthma resulted from emphysema,* and that with this came nutritive derangement of the pulmonary tissue. He believed that emphysema rested on a hereditary basis. He also recognized the *association of a type of dyspnea* with *tuberculosis* and said that it was in some cases at least *associated with* the *cough.*

Bostock[24] says, "There is one circumstance in the history of asthma that is strongly suggestive of the idea that *some organic injury of the lung* is *at the root of the asthmatic tendency;* it is, that in the narrative of cases of asthma it will be so frequently found that the *asthma dates from some disease that implicates the lungs* and in such a way as to imply *injury of an organic nature,* though apparently temporary, as for example, *whooping cough, bronchitis,* and *measles.*

"These diseases are beyond a doubt the commonest of all the causes of asthma; a large proportion (as much as 80 per cent) of cases of asthma in the young dates from one or other of them. In two of them a *specific bronchitis forms an essential part of* the *clinical history.* I think this fact does not admit of misinterpretation. I think this *frequent association of asthma with an antecedent,* even *implying organic,* although apparently temporary *injury of the lungs, must have a very important influence on our notions of the etiology of the disease.*

"*A child* reaches the age of ten years and up to that time has never shown any tendency to asthma; it then *has measles and* although it perfectly recovers from the bronchial affection, *from that time forward* it *is liable to* attacks of spasmodic *asthma.* From this I think we cannot but conclude both that this disease, by some change that it works in the organization of the lung, may *leave behind* it *as a legacy a permanent tendency to asthmatic spasm and* that it *may be the sole and efficient cause of the asthma.*

"There is another circumstance that strongly favors the view that the cause of asthma is organic and seated in the lungs themselves; it is the relative frequency of asthma in the two sexes. Purely functional nervous derangements undoubtedly are commoner in women than in men. Men on the other hand are much more exposed than women to sources of lung injury and their lungs are accordingly much more frequently the seat of organic diseases. Now if asthma was primarily nervous and purely functional—if it were a simple neurosis—we ought to find it commoner in women than in men; whereas, according to my experience, men are more frequently the subjects of asthma than women in the proportion of two to one."

Bostock *describes* his own case of *hay fever,* which, with the exception of a single observation of Heberden's, is the first case on record. Careful inquiry by him found histories of but few previous cases. He says, "After this state of the eyes has subsisted for a week or ten days a general *fullness* is experienced *in the head* and particularly about the fore part; to this succeeds *irritation of the nose producing sneezing,* which occurs *in fits of extreme violence* coming on at uncertain intervals.

"*To the sneezing is added a further sensation of tightness of the chest and a difficulty of breathing with a general irritation of the fauces and trachea.* There is no absolute pain in any part of the chest but feeling of want of room to receive the air necessary for respiration, a huskiness of the voice, and an incapacity of speaking aloud for any time without inconvenience. To these local symptoms are at length added a degree of general indisposition, a great degree of languor, an incapacity for muscular exertion, loss of appetite, emaciation, restless nights often attended with profuse perspiration, the extremities, however, being generally cold.''

Reisseisen,[25] in the early part of the nineteenth century, demonstrated the presence of smooth muscle fibers in the walls of the terminal bronchi and laid a foundation for a deep rooted establishment of the bronchial muscle spasm theory. Prochaska and Reisseisen[26] found that in a living animal with the chest open, the lungs occupied a smaller area than in the dead animal, proving, they thought, that the lungs have muscle tissue.

Wood[27] in reference to nervous or dry asthma in contradistinction to humid or common asthma, as he calls them, says: ''We can trace the disease to a morbid structure of the chest, to an *irritable condition of the bronchial vessels* or parenchyma of the lungs *produced by a pleuritis or a succession of severe and protracted winter coughs; or to a hereditary taint.* Of the occasional causes, however, we are often in great ignorance and mostly so where the disease appears in its simplest character and totally unconnected with any other affection. In some instances it evidently follows upon a sudden repulsion of cutaneous eruptions; in others on a sudden cessation of edematous swellings in the extremities of cachectic patients; and *not infrequently, on inhaling deleterious exhalations;* most of which we have already noticed as occasional causes of dyspnea and dry or humid cough.''

Gregory[28] says of dry asthma, ''There is no secretion from the lungs in short attacks, but when they continue, mucus is secreted.'' Bouillaud[29] agreed with the views of Rostand that asthma might come from any one of a number of pathological conditions, and admitted too, the possibility of the contraction of the bronchi probably by muscular action.

Williams[30] first demonstrated that a current of electricity passing through the lungs caused contraction thereof. But it was only after a considerable volume of air had been allowed to escape from them that signs of contractility occurred. He thinks a spasm of the bronchial muscle explains asthma and implies the likelihood of a strong psychical factor when he observes, ''*if the* *patient after holding his breath a little while, be desired to breathe again quietly, the spasm will be overcome,* as it were, by surprise, *and the entry of the air into the cells will be heard in a clear* and sometimes puerile *sound.''* Kay[31] advanced the view that a chemical change of the blood in asthma *prevented* its *proper circulation through the pulmonary capillaries.*

Laennec[32] further emphasized the theory of bronchial muscle spasm, and, backed by the force of the reputation gained through his epoch-making discoveries in chest examinations, there is little wonder that it has been so generally accepted. Indeed the tendency of that time would make asthma a concrete and definite entity with muscle spasm as the essential factor. With the new methods of examining the chest *many* soon became sufficiently proficient to *discover that asthmatics had very evident morbid changes of other structures than the finer bronchi.* The thought then developed that asthma was merely an incident developing idiopathically in serious heart, lung, or blood vessel disease. This originated when it was found by the postmortem examination of an asthmatic that there was widespread disease of the organs of the chest. Laennec states definitely that he met with only a very small number of asthmatics in whom there was evidence of pulmonary spasm without any attendant catarrhal affection.

He observed that in patients who exercised sufficiently to produce breathlessness, the respiratory sound was indistinct and frequently imperceptible over the greater part of the chest. *After the individual had rested, the sounds again returned to normal.* He believed that the *congestion had something to do with the contraction* of the bronchi and air cells. He concludes ''that the greater number of asthmatic paroxysms, although depending on several causes combined, are chiefly induced by a primary and momentary alteration in the state of a nervous influence.'' *He found that loud reading and speaking tended to prolong the expiratory acts and to cause the rhonchi and dyspnea to disappear.* He had one patient who had an attack of asthma on going to bed in the dark. It ceased on the appearance of light.

LeFevre,[33] himself *an asthmatic, believed* that *asthma resulted from an irritability of the nerves of the lungs, but* reported that he, as with other cases he had seen, *expectorated large quantities of sputum.* Good[34] speaks of *asthma* resulting *from a ''pleuritis* *or a succession of severe and protracted winter cough.*" Eberle[35] thinks "that it is highly probable that asthma consists essentially in a peculiar irritation of the pneumogastric nerves."

Budd[36] undertook some experimental work to prove the presence of muscle fibers in the bronchi and from his experiments he concludes, "the transverse fibers of the bronchi have been wrongly supposed to be muscular." Budd holds that *asthma* is to a considerable degree *dependent upon heart disease, emphysema, etc.* of the lungs. He says, "There still, however, remain some cases which at present we can only explain by supposing dyspnea to be nervous. It seems probable that the number of such cases will be still further diminished and that *many of those fits of asthma* which we are now forced to consider nervous *will be discovered to depend on some organic change* which has as yet escaped our observation, perhaps on some morbid condition of the blood itself.

"In fits of asthma, really nervous, the difficulty of breathing must result from spasm or from suspension of the normal action of the diaphragm and other muscles of inspiration." Budd did not accept the experimental evidence of contractility of the lung as proving that muscle fibers existed in the bronchi; but he was rather of the opinion that there was a contractility of all the tissues of the lung. Longet[37] believed that he had demonstrated that the bronchial muscles are innervated by the vagi. Worthy[38] says, "*Asthma tends to be increased by the horizontal position and is brought on by anything which tends to fill blood vessels of the mucosa of the bronchi.*"

Dunglison[39] raises the *question* whether there *is* such a condition as "*pure nervous*" *asthma.* He thinks there *probably* is *always some organic factor.* Cannstatt,[40] instead of accepting the bronchial muscle spasm theory, put it but little differently by saying that asthma was a spasm of the breathing organs.

Hirsch[41] said that he had *found sufficient structural lesions in each case of asthma* he had seen *to account for* the *symptoms.* In his opinion the important changes consist in congestion of the central nervous system. Parry[42] suggests that *vascular engorgement of* the *mucous membrane of* the *bronchi produced such tumidity* of it *as to mechanically interfere with* the *passage of* the *air.* Chapman[43] accepts the bronchial muscle spasm theory; he refers to a *preceding catarrhal condition of the respiratory pas-*

*sages and cough* and has observed that *holding the breath and talking quietly and calmly decreases the intensity of the attack.*

Henle[44] considers the imperfect expiration and stenotic sounds as evidence of a paralysis of bronchial muscle. Nooth[45] suffered from *"nervous asthma" for years until he expectorated a shot.* Traube[46] placed the lungs of a freshly killed animal in cold water and found that they then occupied less space than after all vitality had disappeared, thus proving, he thought, that the living lungs had a contracting element other than mere elastic tissue. He believed that stimulation of the central ends of the vagi called forth an inspiratory effort even to the extent of causing tetanus of the diaphragm. He suggests, however, that *asthma may be simply an acute inflammatory condition of the finer bronchioles.* Beau[47] considers *asthma* to be the *result of a particular type of bronchitis, the obstruction and wheezing being from an exudative process.*

Hall and Hall[48] say, "Asthma is a spasmodic contraction of the membranous portion of the windpipe. . . . . In consumption the patient dies because there are not lungs enough to receive sufficient air for the wants of the system; that is, they cannot get enough air in; while *in asthma they cannot get enough air out;* hence asthma and consumption are antagonistic, the former is preventive of the latter and a consumptive is cured on the supervention of asthma." Rognon[49] believed that convulsive asthma and angina pectoris were analogous conditions.

Bergson[50] held to the bronchial muscle spasm theory of asthma. Volkmann[51] tied a tube into the trachea of an animal and set a candle before the opening and then stimulated the vagus and the flame showed that air was thereby caused to come from the lungs.

Todd[52] believes asthma to be the result of a humor and compares the disease to gout and rheumatism, the difference being that in asthma the materia morbi affects the respiratory center. Crozant[53] regards *bronchial catarrh with a very viscid secretion* as *the cause of asthma.* Walshe[54] suggests that the easy inspiration and difficult expiration are good reasons for assuming a paralysis of the bronchial musculature in at least certain types of asthma. He adheres, however, to the bronchiolar muscle spasm theory to explain most cases of the disease.

Gairdner[55] takes marked exception to Beau's views and upholds the muscle spasm theory. Donders[56] found that the vital tonus of the lungs amounted to only one-fourth of their contractile energy. Romberg[57] argued in favor of the bronchial muscle theory but thought that there might be *a number of factors* back of this which simply found expression in spasm of the muscle. Wintrich[58] favors the view that spasm of the diaphragm is the essential factor. Duchenne[59] was able to demonstrate that electrical stimulation of the phrenic nerves caused tetanus of the diaphragm, and on learning of a patient who had a supposed rheumatic attack producing apparent tetanus of the diaphragm, fabricated the theory that a tonic spasm of the diaphragm was the principal cause of asthmatic paroxysms.

Biermer,[60] in a very exhaustive article on diseases of the respiratory passages, says that *asthma* is *the result of a swelling of the bronchial mucosa* and a consequent obstruction of the smaller bronchi; the residual air in the alveoli then develops a greater tension and causes thereby a reflex spasm of the bronchial musculature. He reports a patient whose *asthmatic seizures ended after the expectoration of a small feather.*

De la Berge and Monneret[61] stated that it seems *impossible that* the *expectorating of a half gallon of thready sputum could be a symptom of nervous asthma.* Andral[62] held that there was such a condition as "nervous" asthma and in one instance at least, expressed his opinion that it might have come from a "metastasis of rheumatism to the lungs." He believed that the bronchial muscle was the essential element, and this contracted from an irritation of the pneumogastric and phrenic nerves. "The *irritation* in some cases at least, *resulted from enlarged bronchial glands,*" he says. Théry[63] believed asthma to be a spasm of the bronchi for the purpose of getting rid of irritating material. Knaut[64] connected a *water manometer with the trachea* and found, as a rule, that there was a *slight ascension of the water as* the *vagi were stimulated.*

Benvenisti[65] took the position that there must be *definite pathologic processes at the bottom of asthma even though often undiscoverable.* Virchow[66] thought the elastic tissue of the lungs in asthma undergoes a change by softening and absorption. Pridham[67] says as regards sex and asthma, about 80 per cent are men, and in his series, 90 per cent had a hereditary base. He holds that many cases result from improper diet.

Smith[68] argues that *dyspnea causes congestion in the lungs. He asserts blood is inspired into the chest and hence if the air tract is obstructed, proportionately more blood is taken in.* Duclos[69] considers asthma to be a manifestation from the air tubes of a herpetic diathesis, the varieties of asthma corresponding with various forms of skin diseases. Merkel,[70] after an exhaustive survey of the literature of asthma, comes to the following conclusions: (1) Asthma is an affection of the bronchi caused by a neurosis or by an overstimulation of the nerves of the respiratory system. (2) The cramps are sometimes useful for the purpose of preventing the entrance of foreign bodies into the respiratory tract. (3) But from various causes this function may be exercised when it is of no benefit or use. (4) The spasm involves the muscles of respiration. (5) *Bronchorrhea, bronchitis,* dilation of the bronchi, *and congestion commonly result.* (6) *Asthma is usually complicated by catarrh, emphysema, and heart disease.* (7) Treatment is most efficacious if directed toward the nervous system. (8) *Inhalations are the most efficacious treatment.* (9) The location of the neurosis cannot be stated but on that account cannot be denied.

Kidd[71] dwells on the *distention of* the *chest,* the tonic spasm of all the inspiratory muscles, the bronchiolar muscles and the *voluntary effort to expire,* and says that "as soon as the effort to expire is discontinued, the muscles of inspiration, like so many bands of india rubber, distend the chest again." The spasm results, he believes, from some morbid condition in the medulla.

Rosenthal[72] came to the conclusion that the *stimulation of the vagi had* little or *no effect upon the respiration.* Sanderson[73] explained the asthmatic attack on the assumption that there is a marked relaxation of the larynx allowing the vocal cords to approximate each other and thus interfere with the passage of air.

Rügenberg[74] showed that a stimulation of the vagi causing a rise of the intratracheal pressure was in no wise due to the contraction of bronchial muscle but of the esophagus.

Johnson[75] explains the hemoptysis which sometimes occurs by saying: "*At whatever point in the pulmonary circulation the arrest took place, it would retrograde upon the systemic venous* *system, and since the bronchial veins are tributary to this system, it would ultimately retrograde upon them; and thus would be produced congestion and partial stasis, first of the bronchial venules and then of the bronchial capillaries.*"

Salter[76] holds that the pathologic conditions are in the nervous system—the pneumogastric, other nerves, or the nerve centers—and these either reflexly or directly cause a spasmodic contraction of the bronchial muscle. He speaks of the incidence of *venous congestion.* Quoting from him, "I am inclined to think that the exact seat of the obstruction is in the minute venules just where the blood is passing from the capillaries into the pulmonary veins and my reasons are these:—the cause of the stoppage in the blood . . . . not being properly decarbonized. Now the capillaries are the seat of its decarbonization; it is not, therefore, until it leaves them and arrives at the ultimate pulmonary venous radicles that it becomes what it should not be—venous blood, where it ought to be arterial. That point, then, where its defective arterialization must be first recognized, must be the point of its arrest."

Salter gives the following splendid picture of the physiology of asthma: "*If we could see into an asthmatic during a fit we should see pulmonary venous congestion, distended right heart, large veins full and a scant supply of arterialized blood finding its way to the left ventricle.*"

Ringer[77] found that in the hours succeeding a fit there was a marked diminution of urea and chlorides in the urine, indicating, he believed, some profound disturbance in metabolism. Aitken[78] says *asthma leads to dilated right heart and emphysema.* Wintüch[79] found that the vital tonus of the lungs amounted to one-fifth of their total contractile energy and showed that, though the bronchi may be contracted, the elasticity of the air vesicles is still sufficient to expel the air. Sée[80] expresses the opinion that *asthma exists, a sequence to bronchitis, but in a percentage of the cases the bronchitis is masked; there is also emphysema.* A neurosis of the vagi, he thinks, may be a primary factor. He says the *attacks develop* rapidly but usually *not quicker than in a half an hour.*

Von Bamberger[81] says, "The most frequent and the most influential, though not the only cause of spasmodic asthma is a spasm of the muscles of expiration alone." Villemin[82] believed that the *bronchial mucosa* was *predisposed to the accumulation of blood, thus converting it into a sort of erectile tissue.* Fuller[83] divides asthma into spasmodic, where the cause lies in a spasm of the bronchial muscles; paralytic, where the bronchial muscles are paralyzed and the dyspnea is expiratory, more constant, and less spasmodic; and nervous, where abnormalities of the blood are productive of an apparent distress in breathing. Trousseau[84] viewed *asthma* as a neurosis but recognized that *frequently* it was *associated with tuberculosis.* He also saw that *emphysema developed with asthma.*

Breuer[85] weaves a theory that there is an automatic control of breathing through the vagi and that the stretching of the alveolar walls stimulates expiration and hinders inspiration. An increasing of the total lung volume, he thinks, would tend to stimulate expiration rather than inspiration.

Greenhaw[86] speaks of *asthma following bronchitis* and thinks it is rare for the truly spasmodic form to do so. *Paul Bert*[87] was able to demonstrate that an application of stimuli to the vagi produced definite contractions of the lungs but so feebly and slowly that he *concludes* that the muscle had no share in the mechanism of respiration. Section of the vagi caused paralysis of the bronchial muscles, but had no influence on the action of the lungs. He definitely concluded that it was *idle to base an explanation of spasmodic asthma on the bronchial muscle.*

Biermer[88] contends in favor of the bronchial muscle theory. Voltolini,[89] in 1871, found a case with *nasal polyps,* the *removal* of which *cured* the *asthma.* Schiff,[90] by a series of complicated tests, thought he was able to demonstrate contractions of the vesicles and lung tissues generally as well as of the bronchioles. Jaccoud[91] believed that spasm, both of the bronchial muscle and of the external muscles of respiration, is essential to the production of asthma. Von Leyden[92] discovered *crystals in the sputum of asthmatics* and fabricated the theory that these crystals by lodging in the diseased membrane, are essential factors in the production of the attacks. Popoff[93] found that *an introduction of fungi into the air passages produced no effect unless there previously existed an inflammatory condition*—and this was rarely lacking in an asthmatic—in *which cases the fungi produced a dyspnea.* Kussmaul[94] voiced a view previously advanced claiming the stenotic signs, râles, dyspnea, etc., to be evidence of a paralysis of the bronchial muscles. Haring[95] reiterated the theory of Traube putting *special stress upon the acute catarrhal condition of the bronchi.*

Blackley[96] was the first to demonstrate that *pollen* when placed *upon mucous surfaces caused edema, redness, etc.,* and that it could pass through semipermeable membranes and *seemed to be the cause of asthma;* he held that the pollen might be transmitted a long distance thus explaining many heretofore unexplained attacks of asthma. Thorowgood[97] says asthma is the result of a spasm of the muscles of the bronchi and that the difficulty in breathing is to the lungs what colic is to the bowels and what angina pectoris is to the heart. Toeplitz,[98] in some experimental work to establish whether a contraction of the bronchial muscles resulted from stimulation of the vagi, came to a conclusion, as had Rügenberg, that what had been interpreted as being a contraction of the bronchial muscles was in reality a contraction of the esophagus and adjacent structures. Lebert[99] accepted the theory which held a spastic condition of the muscles of respiration to be responsible for asthma. On the findings of Laennec that a patient had asthma in the dark, Lebert advised the use of as many candles as possible in the rooms of asthmatics. After years of experience he was still inclined to admit the possibility of a *purely nervous asthma* but stated such distinction was made *less often in later years of his practice than in the earlier.* Hänisch[100] reported *pathologic conditions in the nose of an asthmatic,* the removal of which cured the patient.

Störk[101] observed that the *mucous membrane of the trachea and larynx is markedly hyperemic during attacks of asthma.* Gerlach,[102] by taking the lungs entirely out of the body, connecting them with a water manometer and then causing the bronchial muscle to contract, was able to obtain a consistent rise of 1.0 mm. in the manometer. In one exceptional case he got a rise of 6.0 mm., and in another 4.0 mm.

Riegel,[103] after thorough consideration of the extensive literature, concludes that while he is willing to concede a more important role to the fluxional element in the production of bronchial asthma and to admit that *the acute tumefaction of the mucous membrane of the bronchioles is the primary element,* he considers it going too far to endeavor to explain the entire symptomatic picture by these conditions alone. This explanation may suffice perhaps for very mild grades of the affection, but that the severer grades—in which the patient forcibly struggles for air; in which, despite the assistance of all the auxiliary muscles of respiration, he is still tortured with the most painful hunger for air, so that the dread of death evinces itself; and in which phenomena of the intensest pulmonary dilatation are developed within a short period—can be explained by the mere tumefaction of the mucous membrane appears to him improbable. Here a second factor must be associated, and that this can be only the spastic element is evident to him.

Schmidt[104] reported cases which appeared to result from lesions remote from the respiratory system. Weber[105] believed an *analogy to exist between stoppage of the nose from "colds" and difficult asthmatic breathing.* He argued that the *bronchial muscle theory did not satisfactorily explain the facts* and he taught that a *paralysis of the vasomotor nerves of the vessels of the bronchial mucous membrane explained the dyspnea.*

Delafield[106] speaks of *bronchitis, emphysema, and mild dyspnea* as being the *forerunners of spasmodic asthma.* Berkart[107] says: "*Asthma* is a symptom, and as such, *accompanies* the idiopathic forms of *chronic bronchitis and emphysema as well as* those that complicate the *various cardiac and pulmonary affections.* . . . . *The anatomical changes peculiar to these affections, (chronic bronchitis and emphysema), are not only slow and latent but even after their complete development, they are so imperfectly accessible to diagnosis as to appear quite out of proportion to the intensity of their symptoms. Those asthmatic seizures are, therefore, always the most conspicuous, after a time even the sole indication of the pathological conditions that take place in the lungs;* and hence they possess all the clinical importance of a substantive disease and require a detailed account of their nature and origin." Hartmann,[108] Schaefer,[109] Porter,[110] and others reported cases of *asthma relieved by the removal of polyps and other pathologic conditions of the nose.* Bokai[111] repeated the experiments and confirmed the findings of Gerlach.

Yeo[112] promulgated the hypothesis that bronchial asthma is much the same sort of distention of the chest as may be of the abdomen in hysteria. He speaks of the great value in one instance of the use of the induced current. Smith[113] suggests that *diminished air pressure in the lower air passages induced by nasal obstruction may be the cause of hyperemia and a supersecretion from the bronchial mucosa, which in turn cause asthma.*

Fränkel[114] believes that the *polyps do not directly cause asthma but* that *changes therefrom* in the nose reflexly *produce it.* Daly[115] calls attention to the *relation between hay fever and asthma.* Bresgen[116] views *asthma* as *dependent upon nasal catarrh.* Unger[117] held that the *cause must lie in a capillary fibrinous bronchitis.* Fothergill[118] says *chronic bronchitis* may be linked with acute spasm of the bronchiolar muscle *causing asthma.*

Riegel and Edinger,[119] from work in which they undertook to prove the theory of bronchial muscle spasm as the cause of asthma, conclude that a spasm of the diaphragm is more likely to be the cause. But they also conclude that *some disturbance of the circulatory apparatus, especially in the bronchial mucosa, is absolutely essential to have the usual findings of asthma.* They say *the practice has been to attack the problems connected with spasm of bronchial muscle and its innervation rather than the problem of asthma itself.*

Bretonneau[120] thought that the *attacks of difficult breathing are caused by violent congestion of the lungs* and are preceded by aura as are epileptic seizures. Curschmann[121] concluded that an *exudative bronchiolitis* was *always primary* to bronchiolar muscle spasm. Trousseau[122] expressed the opinion that asthma is a diathetic neurosis reflected through the bronchial muscles as a spasm. Williams[123] after speaking of the *influence on asthma of dust, odors, dampness, climatic changes, animals, etc., says: "Far more general and intelligible in its action is bronchial inflammation, which is the cause of 80 per cent of asthmatic cases. It frequently happens that after whooping cough, measles, or infantile bronchitis, the tendency toward asthma begins to appear."* Roe[124] reported *cases cured through treatment of pathologic conditions of the nose.* Seiler[125] had one case in which an *attack* was *induced by touching certain foci in the nose. Cauterization of these points relieved the patient.* Frothingham[126] is convinced that an *inflammatory area of the upper respiratory tract is more than likely to involve the bronchi and thus be responsible for the asthma.*

Schnitzler[127] found an *interdependence between asthma and nasal pathology* and says *polyps* are *usually important elements.* MacGillavry[128] obtained experimental evidence that stimulation of the vagi caused contraction of the bronchial muscles. Roy and Brown[129] stimulated the central end of one vagus leaving the other intact and obtained expansion of the bronchi. Giddings[130] says that simple embarrassment of breathing was designated by the earlier writers as dyspnea, whereas, if wheezing existed, it was termed asthma.

Sir Andrew Clark[131] held *asthma* to be *from* a *swelling of* the *bronchial mucosa* analogous to the swelling of the skin in nettle rash, and that the difficult inspiration because of the swelling caused a tetanic contraction of the muscles of the bronchi. Quoting from him, "When the inspiratory effort closes and the expiratory recoil begins and is continued by the muscles of forced expiration, the smaller bronchi, more especially those containing mucous wheals, are compressed and all the passages are relaxed and lose their straight direction. Thus the egress of air is greatly hindered and the act of expiration so much prolonged that it is sometimes suddenly interrupted and prematurely closed by the violent inspiratory efforts originated in the respiratory nerve centers through the circulation of imperfectly oxidated and decarbonized blood. In this way inspiration gains upon expiration; the alveoli are distended with air; the diaphragm is depressed; the chest in all its dimensions is dilated; breathing becomes more and more difficult; death seems imminent; and the paroxysm is at its height."

Flint[132] held bronchiolar muscle spasm to be the only essential cause of asthma. Böcker[133] believes that *nasal polyps* are *comparatively infrequent in asthma;* that the *cause* is rather *some direct irritation of the lining membrane of the bronchi resulting in a bronchitis; and that the hyperemia and swelling cause the dyspnea.*

Bosworth[134] advanced the view that hay fever is a vasomotor rhinitis and that *asthma is* dependent on three things: (1) a neurotic temperament, which, he says, was first demonstrated by Salter; (2) a *diseased condition of* the *nasal mucous membrane;* and (3) some obscure substance of the atmosphere exciting the paroxysms. He contends, "The lesion in a paroxysm of *asthma* is *a vasomotor paralysis of the blood vessels supplying the bronchial* *mucous membrane, and not a bronchial spasm.*" He continues, "The blood supply in the nose being regulated by the same vasomotor tracts as those which regulate the blood supply of the bronchial tubes, a disturbance in one region is liable to be followed by a disturbance of the others; a morbid condition in one region renders the others especially susceptible to disease processes. It would be a very broad statement to make that all cases of asthma find their predisposing cause in intranasal diseases, and yet I am very confident that it is very likely if not entirely true."

Krause[135] thinks that nose lesions produce no more effect in asthma than in other neuroses. Woakes[136] considers asthma to be a "storm of reflex annoyances." He goes on to say, however, "If the history of a patient at the onset of an attack of nasal *asthma* be carefully inquired into it will be found *usually following a severe 'cold' in the head or a succession of such 'colds.'*" Glasgow[137] says, "I consider *asthma* to be *a disorder of vascular irritability;* that the *paroxysm is directly due to a partial occlusion or cylindrical narrowing of the lumen of the bronchi through the swelling of the bronchial mucous membrane,* and that this swelling is caused by a vasomotor spasm of the arterioles with a saturation of the tissues by the liquor sanguinis."

Bosworth[138] says, "Just as far as we can cure nasal diseases, just so far can we cure asthma." This author believes that the *nasal obstruction causes a diminished air pressure of the lower respiratory passages which leads to dilatation of the blood vessels of the mucosa and lessened vasomotor control, producing* in the nose, hay fever; and in the bronchi, *asthma.*

Sandmann[139] interpreted differently the results of those who obtained what they took to be contraction of the bronchiolar muscles by the vagus stimulation, holding that the *evidence* of muscle contraction *was in reality more a complete filling of the blood vessels of the lungs.*

Levy[140] suggested that the control of respiration is through a tonus existing in the vagi. Inspiration, he said, results from stimuli arising when the alveoli have become distended. This was probably the origin of the vagotonia theory of asthma.

Lazarus,[141] from experiments on rabbits, came to the conclusion that both bronchospasm and *catarrh* are *essential* factors *in asthma.* Baumgarten[142] views *asthma* as a neurosis *with morbid* *changes in the nose* causing reflex bronchial muscle spasm. Einthoven[143] reported experiments which have been generally accepted as proving that the stimulation of the vagi caused the muscles to contract. Talma[144] held that *the location and character of the râles heard in an asthmatic are such that they could not come directly from the contraction of the bronchiolar muscle.* He thought, however, that the *circulatory changes in the bronchi* are secondary, that asthma is a spasm of the bronchiolar muscle fibers which are under control of the will; hence *the psychic factor is of prime importance.*

Kyle[145] writes, "Granting that *asthma* be *due to vasomotor paralysis* and bronchial spasm, and admitting the alteration of the nerve centers with predisposition to nervous disturbance in the bronchial region, it is fair to assume that nasal as well as other forms of peripheral irritation may reflexly produce the asthmatic paroxysm."

Ball[146] says many *asthmatics* are *subject to attacks of sneezing.* Quoting from him, "*Not only definite typical spasmodic asthma, but chronic conditions, more often classed as chronic bronchitis where the symptoms are tightness of the chest, cough, and sibilant râles, may arise from intranasal disease.*"

Pawinski[147] describes a type of *asthma due to enlarged prostate* and says the attack can be cut short by catheterization of the bladder. Aufrecht,[148] discoverer of the muscle layers in the bronchioles, admits that the muscles of the bronchi may cause a contraction of the bronchioles, but thinks *asthma is more likely caused by catarrh of the finer bronchi.* Audebert[149] says *asthma redoubles in intensity during pregnancy* of the afflicted, being especially severe at time of confinement.

Kingscote[150] regards asthma as a symptom of some condition just as headache, coughs, and epileptic convulsions are symptoms. He thinks the cause of asthma lies in some tissue or tissues affecting the vagi or sympathetic nervous system. He bases this conclusion on the observation that when the left vagus of an animal is cut and the proximal end is stimulated, an asthmatic condition is simulated in the right lung, and the right half of the diaphragm is thrown into spasmodic contraction. He writes, "There are, however, *three pretty constant factors in cases of asthma of long standing;* these *are cardiac dilatation, acute vesicular emphysema, and chronic congestion of the liver.*''

Solis-Cohen[151] holds that asthma results from a *bronchial spasm* and says this *is* both muscular and *vascular*. The latter condition, he thinks, is of an *urticarial nature or a ''vascular ataxia,''* more especially of the pulmonary vessels than of the bronchial.

De Luca[152] opined that the *narrowing of bronchial caliber in asthma is from circulatory disturbance* plus spasm of bronchial muscle and that the primary factor is a hyperstimulation or excitability of certain bulbar centers, especially the vasomotor. He says the asthmatic attack may be the clinical equivalent of some other neurosis. Farrell[153] is strong in his belief that all or nearly all asthma has a reflex origin in the nose.

Watson-Williams[154] says, ''*Asthmatic attacks are generally preceded by, or accompanied by sneezing and rhinorrhea or may alternate with,* replace, or be replaced by paroxysmal sneezing. . . . . Just as bronchitis, emphysema, and other pathological conditions are a usual consequence of frequently recurring attacks in chronic asthmatics, so we not unnaturally observe as a consequence of the nasal phenomena of asthma, hypertrophic rhinitis, waterlogged mucous membrane, and perhaps even mucous polyps, these nasal affections being often the consequence and not the cause of asthma.

''We find that *there are particularly sensitive areas on the nasal mucosa which, when probed, give rise to violent cough.* I do not allude to the simple cough reflex obtained on probing many normal cases and which may also be excited in many persons by a cotton wad probe or plug in the external auditory meatus. By the *appropriate treatment of these* and other intranasal conditions, I have *obtained successful results.* Many cases have been immensely relieved, and some cured.

''Speaking generally, I have found that cases of inherited asthma are much less frequently due to nasal causes than the acquired forms, and it cannot be too strongly emphasized that the existence of any of these nasal abnormalities in an asthmatic patient does not necessarily imply that they are causal factors.''

Jack[155] considers asthma a symptom of an abnormal biochemical and complex pathologic process originating usually in the intestinal canal. Quoting from him, ''I have found three pathological lesions in the blood that will produce asthma; namely, lymphocytosis, the asthmatic leucocytosis, and the anemic variety." He had *not found a case of asthma due wholly to nasal disease.*

Murdoch[156] reports a case due to absence of hydrochloric acid in the stomach. Lemonnyer[157] thinks that in several cases he has demonstrated the relation of asthma to arthritis and to eczema. Einhorn[158] recognizes "dyspeptic asthma," having seen 31 cases. He says the *attacks may come on immediately after eating or two or three hours afterward,* either spontaneously *or after exercise.* McDonald[159] found that those cases of *asthma in which sneezing had been most prominent* experienced relief from nose operations. Gradle[160] writes, "*Asthma depends on pulmonary lesions (emphysema), cardiac, or renal disease* and is in no way connected with the nose. But it is equally positive that there are instances of typical asthmatic attacks which result from nasal anomalies and are permanently cured by their removal."

Hoffmann[161] thinks that *asthma* is generally understood to be a "neurosis in the domain of the respiratory nerves which shows itself by attacks of dyspnea *with characteristic secretion and distention of the lungs.* The affection is perhaps a pathological change in the respiratory center in the medulla, at least in most cases. In other cases there may be a definite area which directly affects the respiratory center. In yet others the hyperirritability of the respiratory mucosa may be affected, or the entire nervous system be at fault." He therefore terms asthma "a reflex neurosis."

Sihle[162] says asthma is a neurosis of the systems of respiration and circulation and that there are four special points: (1) a hypertonia of the smooth muscle fibers of the respiratory tract; (2) a hypertonia of the circulatory system including the heart; (3) a nervous *bronchial secretion; and (4) a fluxionary hyperemia of the bronchial mucous membranes.*

Brodie and Dixon[163] performed many very ingenious experiments to prove asthma the result of bronchial spasm. They found that a stimulation of the peripheral end of the divided vagus caused a reduction of the amount of air entering and leaving the lung. *Unless some alteration was made in the rhythm or force of the artificial respiration, there was no tendency to inflation of the lung; rather was there a tendency to deflation. But, by increasing the force of the inspiratory blast, or by closing the* *tracheal cannula to a greater extent, or by shortening the time of expiration and lengthening the time of inspiration, a proportional inflation of the lung was caused.* The authors assume that the power of inspiration is greater than that of expiration in man and that the asthmatic is striving to get air into the chest rather than to get it out.

Adams[164] classes asthma with urticaria, epilepsy, etc., and thinks that all are due to endogenous toxins bred in overfed muscles imperfectly exercised. Johnston[165] accepts the bronchial muscle spasm theory but holds that secondary *vascular changes must exist.* Francis[166] believed an asthmatic has a spot on the nasal septum from which spring stimuli reflexly causing the attacks. He found that cases with nasal polyps received the greatest benefit by leaving the polyps alone and treating the septum. Stanley[167] thinks asthma in infants is infrequent and regards attacks so-called as really a bronchitis of spasmodic character.

MacDonald[168] made observations that the *removal of an obstruction from the upper respiratory passages may relieve asthma* and that in the absence of such, *treating the diseased mucosa may effect the same end.* West[169] says *nasal abnormalities commonly cause mouth breathing. Air enters the passages unwarmed and the mouth and pharynx become dry and irritable; chronic pharyngitis commonly results; and from this, bronchitis is but a step.* He emphasizes the importance of the irritative or reflex factors in association with asthma. He writes, "*Cough, often paroxysmal in character, is common* with affections of the nose as it is with those of the throat. *Another affection* which naturally suggests itself *is paroxysmal sneezing.* Beside these, there are various subjective sensations to which nasal affections give rise; for example, sensations of *tightness in the chest or shortness of breath or even dyspnea.*"

Brady[170] reports a number of cases of asthma, well for years after nasal operations. Campbell,[171] while holding the nose often to blame for asthma, says it is frequently *necessary to give intratracheal medication.* Downie[172] found many cases apparently due to nasal disease but emphasized that not all individuals with nasal disease were subject to asthma. Thomson[173] said many patients who thought they had asthma were really suffering from simple dyspnea due to mouth breathing and nasal obstruction. He had one case of asthma associated with Graves' disease; he believes that *suggestion plays a great part with most cases.*

Francis[174] said asthma "is comparatively rare in cases of marked nasal obstruction. . . . . The majority of patients suffering from asthma have their noses in a fairly normal condition. Asthma is sometimes aggravated by a return to free nasal breathing." He again states that best results come from treating the nose without doing operative work. Watson-Williams[175] believed spasmodic asthma to be a neurosis. He never relies on nasal treatment alone to cure the patient, but advises systemic tonic treatment as well.

Spicer[176] writes, "*One of the most powerful exciting causes is the excessive abnormal variations of air tension brought about by breathing through partially obstructed or insufficiently patent nasal channels. This leads to rarefaction of air in the respiratory tract and a dry cupping of the mucosa. The membrane becomes congested, edematous, waterlogged, and ultimately hyperplastic. Its vitality becomes relatively low, and a catarrhal inflammation from a pharyngitis, laryngitis, bronchitis, pneumonia, etc., results; and a condition develops predisposing to tuberculosis. On chronic catarrhal pulmonary conditions, asthmatic symptoms often supervene.*"

Haring[177] lays especial stress upon instability of the nervous system. He says the *attack* is started usually *from a peripheral cause—in bladder, rectum, stomach, or elsewhere.* Brown[178] said *mouth breathing had much to do with asthma,* and that this could be prevented at night by placing a rubber dam between the teeth and lips. Tilley[179] had been astonished at the improvement in some cases by cauterization of the anterior point of the middle turbinate. Smurthwaite[180] says most cases of asthma are not "pure asthma" and hence he preferred the term pseudoasthma.

Newcomb[181] thought "there were so many factors in the neurotic state that one should be cautious in deciding results from any form of treatment, as many results had been obtained from different methods of treatment. Simple alteration of conditions, as a change of sleeping room from one built of wood to one built of brick and change of pillows had both removed symptoms of asthma."

Crandall[182] says *most cases in children date from the childhood epidemics.* Stolkind[183] reports three cases of asthma in children, two of whom had *asthmatic ancestry* and the third a *tuberculous father.* Jack[184] again proclaims his view that asthma results from a toxemia usually due to indiscretion in diet. Holt[185] says, "*Most children who have asthma in winter and spring are sufferers from repeated attacks of bronchitis, the beginning often being whooping cough or measles.*"

Jennings[186] reports that spraying the nose with adrenalin set up an attack. LaFétra[187] found that 27 of 43 asthmatic children had *definite bronchial inflammations preceding asthma.* Fränkel[188] *attributes asthma* to spasm of the muscle fibers plus the effect of *tenacious mucus* and thinks mere *catarrh* could not possibly be responsible for the suddenness of the attack, but that it might produce muscle spasm.

Dünges[189] says *asthma* sometimes *comes with tuberculosis,* but only when there exists a neuropathic tendency, and that ordinarily, tuberculosis does not predispose to asthma. Barbarin[190] says that in children *asthma begins* first *as a severe capillary bronchitis or bronchopneumonia; after which come chronic bronchitis, cardiac dilatation, emphysema, and then asthma* as a neuroarthritic diathesis.

Bayet,[191] in an essay on the relationship of some asthmatic affections to cutaneous outbreaks, concludes as follows: "(1) It is incontestable that in certain cases there may exist a very marked alternation between asthma and the cutaneous affections which accompany it. (2) In certain cases this alternation is observed only when the case is watched for over a considerable period. It is not immediate. The sudden disappearance of the dermatosis has a marked influence on the attack. It is noted that, taken together, the periods of inactivity in the cutaneous manifestations are accompanied by an aggravation of the respiratory symptoms. (3) In certain cases this alternation is not seen. (4) In others, the exacerbations of asthma are accompanied by aggravation of the skin symptoms. It is probable, too, that there exist still other types of relationship between nervous asthma and the dermatoses which accompany it. (5) The relationships which bind asthma to dermatoses are not the same for the whole course of the disease. The alternation or balance may lose its distinctive character. At a given moment the two affections may simultaneously diminish. (6) The physician should treat all dermatoses in an asthmatic and he is at liberty to cause a reappearance of the neurodermatitis if curing the skin affection brings about too violent a return of the asthma.''

Steavenson[192] attributes the expansion of the chest in asthma to ''the preponderantly active muscles of inspiration overpowering the weaker expiratory act.'' Campbell[193] thinks distention of the chest occurs because at the height of inspiration the thinner walled bronchioles are at their greatest dilatation, thus favoring the passage of air through obstructed tubes. Hare[194] had one patient who suffered from asthma till 30 years of age, at which time *tuberculosis developed.*

Morison[195] says, in explaining *the sitting position habitual* to asthmatics, ''The inspiratory muscles certainly act more powerfully in this position, and *the blood, flowing towards the right heart, enters it less copiously and thus tends to limit stasis in the pulmonary circuit, for the upright cavohepatic blood column is less easily emptied into the right heart than in the horizontal.* While in this position the cephalic veins drain better into the chest, which is an advantage, the nervous system generally is retarded, which is also an advantage, and allows the left heart more time to deal with the intrathoracic blood.'' This attitude, he says, is best for pulmonary circulation.

Levy[196] writes, ''Asthma is a neurosis depending upon a susceptible or irritable condition of the nervous system, which susceptibility, when influenced by an external or internal irritant, brings about the characteristic phenomena of asthma.'' Nelson[197] takes the view that asthma is due to spasm of the muscle fiber of the bronchioles plus the turgescence of the bronchial mucosa and plus spasmodic action of the diaphragm and other muscles of respiration.

Pieniazek[198] thinks *the muscle spasm theory is untenable and that the whole cause is a swelling of the bronchial mucosa, a sort of hybrid between a catarrh and a pure edema, due to vasomotor paralysis of the finest bronchial venules.*

Galdi [199] reports a case subject to marked vasomotor disturbances of parts of the body other than the bronchi. Avellis[200] accepts the statement that asthma is primarily a neurosis and *pins* his *faith to sanatorium treatment, hygiene, respiratory gymnastics, suggestive therapeutics*, etc. Coggeshall[201] takes the view that inflammation of the mucous membrane of the ethmoidal cells causes an inflammation of the endings of the trigeminus or olfactory nerves and that this secondarily causes an altered activity of the medulla, particularly of the respiratory center. The *result in the bronchi is either a vasomotor disturbance,* or a spasm of the bronchial muscles, or both.

Kohn[202] says it has been learned by experience that *asthma occurs chiefly in people who are of a neurotic temperament.* He thinks the neurosis may result from trauma, intemperance, sexual disturbances, and other factors affecting the respiratory center. Von Jezierski[203] holds that there are two types of *asthma,* one *caused by overfilling of the venules of the bronchial mucosa and* the other *by infiltration of round cells into the mucosa.* Arneill[204] says the *cause of asthma lies in the mucous membrane,* sensitive nerve centers, an external excitant, and the presence in the blood of toxic substances.

Dock[205] is of the opinion that the disease is essentially a reflex neurosis. He emphasizes the importance of exhausting all means for a *diagnosis of the organ or part responsible for the attack.* Robinson[206] has found a number of patients who developed asthma when an eczema disappeared and eczema again with the disappearance of the asthma. From this he concludes that asthma is a blood disease.

Wolf-Eisner[207] found that of *100 asthmatics tested, all but four gave hay fever symptoms when pollen, rubbed up in salt solution, was dropped into the eye.* Rochester [208] takes the view that though asthma may be primarily a neurosis, there is also a concomitant *bronchiolitis with an exudate of mucus.* He is of the opinion that the neurosis arises secondarily from poor oxygenation and autointoxication, both of which come *from the emphysema which naturally follows chronic inflammatory processes of the bronchi and upper air passages.* Imperfect elimination and autointoxication from any source may be the actual causative element.

Gauldrini[209] is of the opinion that asthma is essentially *a hereditary psychic factor.* He compares it to a traumatic psychosis and cites the histories of three typical cases in which the paroxysms came on in each case with the *only appreciable excitant being emotion.* Schadle[210] reported a *case of bronchial asthma; hay fever had been persistent for more than two years and there was* *also a double antrum of Highmore infection.* Permanent relief from all three conditions followed treatment of the infection.

Von Strübing[211] had *healthy students* imitate the breathing of asthmatics and after a time they *succeeded in causing mild wheezing and signs of dry bronchitis much as asthmatics have. After subsequent periods of normal breathing the asthmatic signs passed off.* They found that *"colds" and coughs materially helped to bring about wheezing.* One student also observed that when he developed a "cold" with catarrh of the larger bronchi, the expiratory findings developed irrespective of his occupation and attention. Some six months after practicing the asthmatic breathing, he took a *severe "cold" and bronchitis and* one night he developed a *paroxysm of coughing* which was *followed by an attack of asthma.*

This student then attempted to ascertain if he could cut short an attack by the proper regulation of his breathing. At times this seemed impossible. The harder he tried, the worse the tickling in the larynx became and hence the more severe was the cough. After a while tickling and cough subsided and it became possible for respiration to be more deliberate. The time of *inspiration was lengthened and expiration was made without muscle effort, the wheezing of respiration diminished and the attack ended.*

It was practically a year before the student's health returned to normal. Von Strübing recognized that *most asthmatics have catarrh of the bronchi which may be an extension of an inflammation from the nose or some other part of the respiratory tract.* He says, however, that *certain persons without catarrh of the bronchi may develop coughing and such breathing as will bring on asthma.* Especially does he emphasize the importance of *coughing* as a *cause of* the *asthmatic type of breathing.*

He also mentions, in an indefinite way, the possibility of *circulatory changes in the mucosa following coughing and the asthma-like breathing.* This, he says, may arise much more easily when there is catarrh, as proof of which he cites the well known incidence of wheezing with catarrh of the bronchi. *He says there are individual differences, as, for instance, the intensity of the catarrh, the irritability of the mucosa, the severity of the cough, and in some cases, the patients may regulate the breathing to control the attack.*

Von Strübing could not believe, as did Talma, that the smooth muscle fibers of the bronchi could be controlled by the will. *He also could not see why the contraction of the muscles should always occur in expiration.* He assumed that *in some way* the *forced respiration through pressure affected the mucosa which was inflamed.* Von Strübing says that when the nose has irritable foci, the touching of which produces asthma, it is really the *coughing* and not the sneezing which produces the asthma. He also suggests the possibility that the air cannot get out of the alveoli because the *pressure collapses the finer bronchioles.* But the remainder of the question is unsettled in his own mind.

Soca[212] takes the view that the essential pathology lies in the respiratory center producing spasm of the diaphragm, which leads to *emphysema* and this, in turn, produces the *dyspnea* and *bronchitis* which are the two *essential factors.* The *asthma,* he says, is *characterized by three things; emphysema, dyspnea, and bronchitis.* The author holds that the *tuberculous constitution* is also *that of* the *asthmatic* and that there is in most cases an *interdependence of asthma on tuberculosis.* He reviews a series of 700 cases of asthma, and *evidences of tuberculosis* were found *in* nearly *all.*

Behrens[213] writes of a man who had *asthma, bronchitis,* and trigeminal neuralgia which he thinks resulted *from vasomotor paralysis* secondary to irritation of the nerves of the nose. Smith[214] holds to the theory of bronchial muscle spasm plus a vagotonia, and says while *there is a vasomotor disturbance of the mucosa of the respiratory tract,* this change does not directly cause the asthma; but the *engorged mucosa* pressing upon the asthmogenic points in the nasal fossæ originates stimuli which are reflected through the pneumogastrics and which *produce the paroxysms.*

Zuelzer[215] believes that asthma results from an "expansion of the lung" through vagi irrigations. He thinks there is in addition a *swelling of* the *bronchial mucosa* and possibly a bronchial muscle spasm. Cautley[216] in discussing the prophylaxis of asthma emphasized the *importance of* (1) recognizing and properly treating the children who are predisposed to *catarrhal processes* and (2) *guarding against those diseases.* Dünges[217] reported a case that had *attacks when sleeping* upon a sea grass mattress.

Dean[218] is of the opinion that though cases of asthma may be practically cured by some operative procedure in the nose, the two conditions are simply associated rather than being cause and effect. Von Hoesslin[219] says a patient had for years *attacks of air hunger* which *always began with a cough* and a small amount of secretion. He was inclined to the view that the patient had an edema of the lungs, that his condition depended to a great extent upon cardiac embarrassment and that this is true in many cases of asthma.

Oxley[220] reports *asthma resulting after the inspiration of a fragment of a tooth* and its ceasing after the tooth was expectorated. Waugh[221] had seen a *number of cases* which *developed after repeated attacks of influenza.* Kitzmiller[222] observed that his own *asthma came on* especially *after lying in a horizontal position* for a time.

Grossmann[223] says we no longer doubt the power of the *bronchial muscle* to contract; but this *contraction cannot be of such strength as to produce grave respiratory disturbances;* and *experimentally it is not possible to produce contraction of the muscle fibers without producing circulatory disturbances,* and clinically both may exist; but *it is possible to have circulatory changes without contraction of the bronchial fibers.* He says further that *the appearance, disappearance, and severity of the respiratory disturbances are parallel with the circulatory changes.*

Hofbauer[224] suggested that asthma may be a manifestation of Basedow's disease. Avellis[225] explains asthma, "especially nervous asthma," on the basis that there is an "Organ Gefühls," a center in the nervous system not as yet located but one which surely exists, disturbance of which causes a desire for greater ventilation of the lungs; and in this way the asthma begins. The cure, he says, rests in the control of the stimuli as by use of belladonna or morphin.

Andrews[226] is of the opinion that *nasal foci causing asthma do so by keeping up a bronchitis.* Lewis[227] reports a man who developed a *"severe purulent rhinitis"* with a frontal sinus becoming infected later. *Five weeks* after its onset, *asthma appeared.* Emptying the sinus of pus always relieved the attacks. Later *the bronchitis became very pronounced and the paroxysms increased in number and severity. When the nose got well, the bronchitis and asthma disappeared.* Bailey[228] reports the *cure of* *asthma by the removal of a swollen middle turbinate allowing free drainage of an infected frontal sinus.* Amos[229] views *asthma* as a *result of bronchitis.*

Nowotny[230] *observed in* three cases *of bronchial asthma by means of the bronchoscope, great swelling and hyperemia of the bronchial mucosa extending to the smaller branches.* He decided that it existed even further than he could see. *The introduction of the bronchoscope caused in every case an abundant expectoration and this, coupled with the cocaine-adrenalin anesthesia, caused cessation of attacks for at least a month.* Goldscheider[231] recognized that *if an asthmatic would give normal time for each phase of the respiratory act, the condition would be improved.* Aboulker[232] reported two patients relieved of asthma by nasal operations.

Ellis[233] says the findings in the sputum and the autopsy lesions in asthmatics are not pathognomonic, being present in other diseases as well, and hence we are forced to regard asthma "as the result of a cause as yet undemonstrable by studies of the lungs of these subjects."

*Von Strümpell*[234] *says if it could be shown at autopsy that the bronchial muscles in this disease are positively hypertrophied, some weight would be added to the bronchial muscle spasm theory; but this has not been found.* He holds that *asthma is a vasomotor secretory disturbance of the bronchial mucosa which, coming on suddenly, causes stenosis.*

Stegmann[235] cites *three cases* all of whom *attribute* their *attacks to "colds."* He calls attention to a certain regularity in the time of the appearance of the attacks and reports that *all three* patients were *cured by suggestive therapeutics.* His opinion seems to be that there is a *strong psychic factor in asthma.*

Möller[236] views asthma as a neurosis of the respiration center which, being stimulated through asthmogenic points at various parts of the body, may cause the disturbance to be manifest. He *advises suggestive therapeutics*—and surgery when indicated. He thinks the *nose* is *frequently at fault.*

Gillette[237] took two injections of diphtheria antitoxin, and for a time, had complete relief from his asthma. He gave a patient the same treatment and death resulted. Langstein[238] reports four cases of eczema, one suffering from asthma, each with an eosinophilia closely resembling that of asthma. Both conditions are classified by him as belonging to the so-called exudative diathesis. He states, however, that the asthma is not influenced by a reduction of salt in the diet as eczema is.

Saenger[239] *found cases of marked emphysema with but little or a cured asthma and others of severe asthma with little or no demonstrable emphysema. This led him to the conclusion that the physical factor in asthma is of great significance.* O'Dwyer[240] says in regard to asthma and the climate of Egypt, "The *personal factor has a most important bearing* on such cases—I had almost said the most important—at any rate it is extremely difficult to anticipate the possible effects of a place on an individual case." McCullough[241] says that Guha, an epidemic disease in Guam attacking children chiefly, produces symptoms characteristic of asthma. The disease is acute and pneumonic in type when affecting the lungs; there is continued fever, hemorrhagic infection of lungs, and intestinal ulceration, but the asthmatic type of breathing is usually not exaggerated.

Treupel[242] holds that *asthma is a psychosis.* For the acute attacks, he advises the ordinary narcotic remedies; but for the asthmatic predisposition, he *recommends drills in breathing,* hydro- and pneumo-therapy, a *change of climate,* etc. But he *emphasizes the value of psychic discipline.* Kirschberg[243] *advises a sharp quick inspiration and a long complete expiration.*

Bronner[244] says that an unstable condition of the respiratory center is present in most cases and he thinks it is the most important factor in the causation of asthma. Arkawin[245] claims to have *found in all cases* in children more or less chronic bronchitis, but he thinks that asthma itself comes from a reflex action.

Auld[246] says, "Any wreckage found postmortem is solely confined to the chest while the nervous system is healthy, and so we may safely affirm that *asthma is a disease of the lungs.*" *He blames* the bronchial muscle, the *congestion of the mucosa, the altered secretions of the mucosa* and an excess of carbon dioxide in the blood for the dyspnea. Granting muscle spasm, he says, "After cessation of the spasm, the disease is still there."

Gay and Southard[247] found that dyspnea resulted in guinea pigs following a second injection of a protein to which the animals had been sensitized. Knopf[248] held that there is a similarity between stuttering and asthma. Maurel[249] says *asthma* in children ***begins*** suddenly *with air hunger and râles all over the chest* and he likens it to, or says it is difficult to distinguish from, edema of the glottis, croup, laryngospasm and diseased tracheobronchial glands.

Moncorgé[250] believes the start of the reflex spasm comes from a toxin or from a deficiency of oxygen in the respiratory center and that asthma is of the nature of a neuroarthritic diathesis. He says it comes on in sleep because of the conjunction of the normal depression of the respiratory activity and the normal increase in the motor excitability of the spinal cord.

Eustis[251] writes, "The fact that I have found evidence of autointoxication in every asthmatic examined by me for four years leads me to believe that during the attacks there is some toxin in the blood which acts similarly to muscarin, or which depresses the respiratory center to such an extent that the reflex stimulation of an *inflamed nasal mucosa* results in a stimulation of the constrictor fibers of the vagus."

Lloyd[252] believes that asthma is essentially a "nervous disease" and is due to spasm of the bronchial muscles with three causative factors, which are: (1) the presence of hypersensitive areas in the nasal mucosa or a special sensitiveness of the gastric mucosa; (2) an irritability of the pulmonary nerve supply; and (3) the *presence* in the air *of* an *irritant—dust, odors, smoke, etc.*

Carmalt-Jones[253] found *a case with an almost pure culture of a certain bacillus,* gram-negative, rounded ends, nonmotile, growing readily on ordinary sugars. The patient had a low opsonic index to the organism and a vaccine was prepared therefrom. The administration of the vaccine benefited him. Jones administered the vaccine to 52 patients and 25 per cent of them were appreciably benefited. He searched for the same organism in many other cases without success. He suggests, however, that this organism may be the cause of "spasmodic" asthma and hopes further researches may prove it. He refers to *asthma* as "that *spasmodic dyspnea, a distressing symptom in many cases of chronic bronchitis.*"

Grossmann[254] found that electrical or mechanical stimulation of the nasal mucosa caused decided disturbance of the cardiac action and that this was followed by *engorgement of the pulmonary vessels.* This, in turn, rendered the *lung tissue rigid, interfering* *seriously with respiration.* There resulted also an increase in the external dimension of the lungs.

Saenger[255] states that five years' experience has confirmed the *benefits of* his method of *training the patients to breathe so as to endure long pauses between the inspirations; the patient may count, blow, whistle, or play on a mouth harmonica; a very important point is to teach him to control the cough, as it is likely to start the attack.*

Miller[256] reports an attack of asthma which developed following a wasp sting in which there was a prompt edematous urticarial swelling of parts of the skin and also of the uvula and pharynx. He evidently thought the wasp's stinger had entered a small vein. But the author stated that the *patient had had a "cold" for some weeks previous* and also that *the asthma came on immediately or shortly after severe sneezing.*

Gennari[257] reported a young woman who had had severe asthma for two or three days preceding the menses. The only pathologic finding was a hypertrophied thyroid. During the attacks the thyroid became more vascular and turgescent. Ordinary treatment was of little avail. The attacks ceased with the appearance of the menses. The administration of thyroiodin reduced the size of the gland to normal and the attacks never appeared again. The author thinks the asthma resulted from a vasomotor neurosis upon which the hyperactive thyroid had a decided influence.

Schmidt[258] found a relationship between lymphatic or neuroarthritic diathesis and asthma, and he thought acetonemia might be partially responsible for the attacks. Halstead[259] observed what he termed *"angioneurotic edema" of the bronchi.* Boellke[260] recommended the use of pyrenol because he said it *primarily improves the bronchitis and* hence *secondarily the asthma.*

Barnes[261] refers to a case whose *attack* followed or *came with a severe coryza, laryngitis, and trachitis.* Butler[262] says, "Asthma has for its essential cause the abnormal excitability of the vagi; hence the spasmodic condition of the muscles which participate in the act of inspiration results. If the excitability of these nerves is very great, only a slight irritation is necessary to provoke a paroxysm of asthma; if on the other hand the excitability is only ordinary, the paroxysm will be caused only by very decided irritation."

French[263] holds that the essential factor exists in a hyperesthesia of the vagi and that polyps in the nose and other foci of irritation are primary accessories to the paroxysm. Günzel[264] takes the view that asthma is a disease of the lungs produced through various sorts of stimuli to the respiratory center of a hypersensitive nervous system.

Dixon[265] says, "For the production of an attack of asthma two things are necessary—a neurotic medulla and a peripheral stimulus as the exciting cause." Wallace,[266] reported *asthma* following the eating of ice cream. The *patient suffered acutely with lachrymation, sneezing, dyspnea and cyanosis.*

Von Terray[267] believes that *asthma results from* a spasm of the bronchiolar muscles plus *exudative vasomotor changes in the mucosa of the bronchi.* Back of all this he thinks is a neurosis. Hertz[268] found that in his own case deep concentration was apt to stave off an impending attack, whereas thinking of it hastened its precipitation.

MacPherson[269] reports three cases in which the initial paroxysms occurred several weeks after an operation on the ethmoid cells. *In* at least *one of the cases,* however, *the author refers to a prolonged attack of respiratory tract inflammation.* M. K. A.[270] reports a case who had been free from asthma for some time and who *took prophylactically* 2000 *units of diphtheria antitoxin. The serum rash and urticaria developed; but no asthma.* A few days later, however, the asthma came on.

Grossmann[271] reports that an electrical or mechanical stimulation of the nasal mucosa produced a functional disturbance in the heart action and a stasis of blood in the lungs; this did not occur if the two branches of the trigeminus or the pneumogastrics were cut. The stasis caused not only an increase in the exterior of the lungs, but a diminution of the space in the bronchi as well. Loss of lung elasticity was also observed whenever the dyspnea became intense.

Auer and Lewis,[272] Anderson and Rosenau,[273] Anderson and Schultz,[274] Biedl and Kraus,[275] and others have observed and repeatedly confirmed the fact that in the anaphylactic reaction in guinea pigs, there is a spasm of the muscles of the bronchioles which so alters the breathing as to simulate asthma in man. Consequently some observers advance and support the theory that asthma is an anaphylactic stimulation of the muscle fibers of the bronchioles.

Auer and Lewis[276] demonstrated that in a guinea pig dead of anaphylactic shock, the lungs were greatly distended and remained so after removal from the body, even when divided into small pieces. This occurred, too, when the animal had been curarized or when it had had its central nervous system destroyed, thus showing the action to be a peripheral one. They found no evidence of edema of the lungs. The authors believed the distention to be due to tonic contraction of the muscles of the finer bronchi.

Meltzer[277] writes, "May we not assume that asthmatics are individuals who are sensitized to a definite protein substance and that the asthmatic attack takes place when the same protein substance invades the body in the same manner? For one form of asthma this has been established experimentally and that is for hay fever asthma. . . . It has been generally accepted by most clinical writers of the present age that the asthmatic attack is due to a tonic contraction of the muscle fibers surrounding the finest bronchial tubes due to stimulation of the peripheral end of the pneumogastric nerves and not to the production of circulatory changes of any kind."

Percepied[278] says that in 40 per cent of his female asthmatics, the attacks came on with or just preceding menstruation. He emphasizes that *in all asthmatics there is a tendency to chronic respiratory tract inflammation* and thinks attention should always be given it. Hall[279] reports a physician who at 35 had *whooping cough and following this, asthma.* Eppinger and Hess[280] have offered the suggestion that bronchial asthma is a general condition of the entire body in which increased tonus of the nervous system is the important factor—the attack itself depending upon vagotonia. Crane[281] views both asthma and hay fever as nasal reflexes.

Brügelmann[282] holds to the theory that the spasm results from an irritation of the respiratory center. The causes may be trauma, toxins, reflexes, or psychoses. He thinks there is an *urticarial condition of the mucous membrane of the bronchi and asthmogenic points in the respiratory tract.* He says since there is no obstruction in the bronchi, the only explanation of the accumulation of air in the chest and the inability to expel it must lie in a morbid condition of the center of respiration in the medulla. Jackson[283] believes that asthma is a neurosis.

Pins[284] differentiates between cardiac dyspnea and asthma by the rhythm of the respiration—there being long inspiration and short expiration in the former, and the reverse in the latter. He thinks the pathology of asthma lies in lowered respiratory force either from inherited weakness of the muscles or from an over accumulation of carbon dioxide which secondarily produces *congestion of the mucosa of the bronchi.*

Melland[285] reports *asthma succeeding hay fever of three years standing.* Commenting on the relief of an attack, he says, "I have thought sometimes that a bad paroxysm of asthma might tend to cure itself by the downward pressure of the diaphragm actually pressing mechanically on the adrenal gland and stimulating it to get rid of adrenalin." He observed that *if an asthmatic held his breath "almost to insensibility" he could then breathe naturally* for one or two breaths.

Yankauer[286] *observed intrabronchial congestion during an attack of asthma.* Von Strümpell[287] advances the view that asthma is comparable to mucous enteritis and migraine, both being expressions of an exudative diathesis. A *psychopathic irritability* also *plays a part* he thinks. Spiesz[288] takes the view that asthma is a reflex neurosis and that the cause is nasal. Rothschild[289] calls attention to the possible connection of the endocrine glands with asthma. Horn[290] concluded from bronchoscopic findings in one case that it is possible to have an almost complete *closure of* a *main bronchus* by tonic cramp of the bronchial muscle and that this is the cause of asthma. Fodor[291] reports a case he had observed for ten years. *Each attack* was *preceded by bronchitis. For two or three days after* the *bronchitis began,* the *breathing remained normal, but gradually the asthmatic type ensued* in spite of the administration of iodide, atropin, etc., and remained for weeks. The patient—as were others he had observed—was subject to urticarial erythema and other evidence of an exudative diathesis. Of another case he cites, the *attacks* also *came on with bronchitis.*

Saenger[292] takes the view that asthma is a traumatic neurosis and *recommends respiration drills* consisting of relatively *rapid* *inspiration* through the nose by use of the abdominal muscles *and slow expiration.* He claims four weeks treatment suffices to cure. Goldschmidt[293] *recognizes* a nervous, a *catarrhal* and a toxic *asthma.* Gerhardt[294] and Romanoff[295] both advance the theory that the *attack* itself *hinders* the *circulation of* the *blood in the lungs because of increased intraalveolar pressure.*

Billard[296] believed that essential *asthma* can be *excited by* "toxalbumins, *pollen, and germs.*" He has seen attacks following the ingestion of sea fish, crustacea, game, etc. He holds that *asthma,* like hay fever and urticaria, is *a phenomenon of anaphylaxis.* Weiss[297] says that without irritability of the respiratory center there is no asthma.

Abrams[298] believes that asthma is due in most instances to spasm of the bronchiolar muscle, but advances the oft repeated suggestion that there may be an *exudative bronchiolitis or a hyperemia of the bronchial mucosa* analogous to urticaria. He argues that the circular fibers of the bronchioles hold air in the alveoli and the longitudinal fibers force it out. He is of the opinion that a firm stroking of the skin causes dilation of the lungs and that a sharp striking of a pleximeter resting upon the chest causes the lung beneath to contract temporarily. If adrenalin is given, the former reflex is reversed.

Grant[299] attempts to explain expiratory dyspnea. He says, during inspiration, *expansion of* the *chest* walls is *accompanied by dilatation of all the hollow structures* therein, *including* the *bronchial tubes.* The reverse occurs in expiration and the *narrow thin walls* of the tubes are further *narrowed,* thus *offering* serious *obstruction to* the *passage of air.* Galebsky[300] reports five cases of typhoid bronchial asthma, all of which he examined by the bronchoscope, *finding in all mucous membrane markedly swollen and edematous, covered with tenacious mucus.* He concludes such conditions probably are the cause of asthma and that spasm of the bronchial musculature or diaphragm, if occurring, is a secondary phenomenon.

Schittenhelm[301] expressed the opinion that there may float in the atmosphere a number of substances which, reaching the air cells, may be responsible for asthma. Dieulafoy[302] held to the view first advanced by Trousseau and Jaccoud which combines the theory of spasm of the bronchial muscle with that of spasm of the external muscles of respiration.

Berkart[303] advances the theory that *asthma* is the *result of an exudative bronchitis,* which, in turn, may be due to a specific organism. He is inclined to feel that the organism is a streptococcus. He holds that *compact masses of tenacious mucus lodge in the bronchi and interfere directly with the passage of air and that expectoration of these plugs always affords relief.*

Freudenthal[304] said, "I am convinced that there are asthmogenous points in the bronchi as well as in the upper respiratory tract." He was of the opinion that the attacks result from stimulation, reflexly or otherwise, of these irritable points. In a bronchus of one case he found a scar-like mass obstructing the entire lumen, and in another an ulcer. He *observed that during the paroxysm the mucosa of the trachea and bronchi was much swollen and congested.*

Anders[305] says, "Asthma is characterized by paroxysmal dyspnea due to contraction of the muscles of the smaller bronchi." Von Strümpell[306] describes asthma under the head of *asthmatic bronchiolitis,* and says, "I am inclined to attach *far greater importance to the varying amounts of swelling of the bronchial mucous membrane* than to a possible tonically contracted state of the musculature of the bronchioles." I quote as follows from Myles:[307] "The peculiar spasm to which the trachea and bronchi are subjected in asthma is a habit spasm due to the *constant state of hyperemia of these parts* and a reflex central irritation."

Neumayer[308] suggests the possiblity that asthma might often be the result of an abnormality of one or the other of the inferior ethmoidal nerves. By means of local anesthesia it can be ascertained which nerve is at fault. He cites five cases in which the nerve was removed. The results were satisfactory, and permanent in two; but in the three others the attacks returned.

Ebstein[309] has had *cases relieved by curing constipation.* He does not believe that all cases of asthma are due to constipation, but advises that this always be looked for. Solow[310] says, "The most plausible theory and the one now accepted by a great majority of the most prominent writers and specialists is the reflex theory; namely, an irritation reflected from the nasal air passages to the small bronchial muscles." He admits, however, that many cases of asthma do not improve after all indicated nasal surgery has been done.

Lemann[311] refers to the infrequency of nasal complications and to the *frequency of obesity.* Maurel[312] describes an attack of *"hay" asthma.* He says it invariably *began as a coryza with all the attendant manifestations and that later râles and dyspnea developed, the patient then gradually becoming asthmatic.* Parker[313] has been using *diphtheria antitoxin* in the treatment of asthma and feels that while it does some good, its *action* is *largely psychical.*

Hedenius[314] had *five patients with tuberculosis and asthma.* He is of the opinion, however, that the two conditions are not interdependent unless in the event that the *asthma may depend upon tuberculous glands.* Comby[315] reports as his experience with 75 cases of asthma in children that "this paroxysmal respiratory neurosis" is not due to adenoids or nasal catarrh and is not influenced by operations on the nose. The *asthma,* he says, *is commonly accompanied by catarrhal bronchitis or violent and repeated sneezing.* Mahomed[316] noticed *one case* who *had attacks brought on by exercise* and who *coughed a great deal and very hard.*

Moschowitz[317] takes the position that anaphylactic disease is invariably associated with an eosinophilia, that asthma is so associated, and, therefore, asthma is the result of anaphylaxis. Imperatori[318] reports a case successfully relieved by nasal operation. Beaudoux,[319] even when no evidence of sinus disease is found by transillumination and intranasal examination, *treats his patients by* irrigation of the sinuses plus the *application* of *drugs which tend to harden the membranes.*

Kafemann[320] relates that he has seen a *very great number* of persons *with nasal pathology and not the slightest trace of asthma and many decided asthmatics with normal noses.* Béal[321] believes there is a definite preasthmatic status which can be recognized. He *emphasizes three factors—the nose, the bronchi, and the intestinal canal.* The essential factor in the nose is sensitiveness to a slight breeze, dust, or falling temperature. In the bronchi, *catarrh is positive, the sputum is usually ropy and viscid, and on slight exertion, respiratory distress appears.* As regards the intestinal factor, there is *susceptibility to reflex irritations which affect respiration* through the pneumogastric.

Kayser[322] holds asthma to be a spasm of the bronchial muscle occurring secondarily to reflex stimuli. Pescatore[323] takes the view that *asthma* is an *exudative bronchial neurosis*. Giffin[324] writes, "The most unusual things will occasionally cure asthma. Looking upon the condition as a spasmodic neurosis, one would, however, expect strange cures. Nasal operations seem to do this if the patients are properly selected." Giffin found in a series of 82 cases *three who were positively tuberculous*.

Sadger[325] says asthma may be dependent upon sexual factors. Barach[326] attempted to demonstrate anaphylactin in the blood of asthmatics. In the three experiments performed, he failed. Hofbauer[327] says *expiration* is *by* the *normal elasticity of lung tissue* plus the use of the auxiliary muscles. These two, he thinks, do not work harmoniously in asthma. A pressing, *forceful expiration* results and this *hinders rather than assists the passage of the air outward.*

Shaw[328] reports the case of a girl subject to asthma who had at the time of the attacks a skin eruption. Detrain[329] holds that asthma is the result of disturbed internal secretions. Allbutt[330] *protests against* the use of the term "*cardiac asthma*" *for* "*cardiac dyspnea,*" *an entirely different thing.* Saunby[331] considers asthma to be a reflex spasm of the inspiratory muscles, chiefly of the diaphragm—the origin of the reflex being anywhere in the body. He concludes that there may also be spasm of the bronchiolar muscle and *turgescence of the mucosa.*

West[332] holds asthma is a neurosis with somewhere in the nervous system an irritable focus, just as in epilepsy, and that peripheral reflexes causing asthma do so only in one who is asthmatic. *Plastic bronchitis,* he says, *may lead to a paroxysmal dyspnea* which might be wrongly diagnosed as asthma.

Ewart[333] says, "Asthma is practically an expiratory stenosis by relative disparity of the respiratory forces and this disparity must grow with the stretching of the expiratory muscles." He thinks the stimuli of the attacks are usually peripheral and that the chief morbid change lies in the vagi. Hunter[334] opines that the spasm of the bronchial muscle is more important than the *congestion.*

Wilson[335] had recently seen a case of numbness of the hands and feet caused, he supposed, by a vasomotor spasm, and sees no reason why asthma might not arise in the same way. Grünbaum[336] found a *case* that was *greatly helped by a vaccine* of the bacillus catarrhalis and the pneumococcus, and allows us to infer that he held these organisms to be the essential etiologic factors.

Carter[337] says asthma is the result of nervous instability. The influence of diet, he thinks, is easily explained on this basis. MacKenzie[338] considers asthma to mean labored breathing and more particularly that form characterized by periodic attacks. He has observed such a type of breathing in conjunction with cardiac disease, and, therefore, calls it "cardiac asthma," in the same sense that other authors refer to nasal, uterine, ovarian and kidney asthma.

Gibson[339] accepts the view suggested some years ago by Williams; namely, that during ordinary respiration there probably is rhythmical dilatation and contraction of the bronchial muscular coat in association with the movements of the larynx, trachea, and nostrils, and that in asthma these movements are simply exaggerated. He says we have two types of asthma: "The first group comprises the cases independent of definite lesions in which paroxysms of characteristic dyspnea occur, sometimes apparently in a spontaneous manner, at other times precipitated by different local irritations—these cases constitute the recognized nosological conception which we term asthma. The second group includes instances with obvious disturbances, as cardiac, pulmonary, excretory, metabolic, or otherwise, from which we can with absolute certainty conclude that the symptom of dyspnea is secondary." He calls attention to the *part played by anger, grief, and other emotions in precipitating attacks.*

Miller[340] thinks asthma is wholly a psychical state and amenable only to suggestion. Smith[341] found that sodium nitrite caused the urates to completely disappear from the urine and he suggests that the reason the nitrites are of benefit may be that they get rid of substances in the blood which cause asthma.

Haworth[342] says, "In the true form it is probable that there is a spasmodic contraction of the muscle fibers of the bronchi, the lessened lumen not being sufficient to accommodate the normal secretions of mucus, hence the râles of varying degree, the 'perles' of Laennec formed of the Curschmann's spirals being rolled up into pellets by the violence of the expiratory and inspiratory efforts." MacDonald[343] reports cardiac disease which developed into periodic dyspnea and this he termed "cardiac asthma." He attributes it to embarrassment of the right heart due to constriction of the coronaries.

Francis[344] says, "If we could get away from this hereditary belief in muscular spasm, and allow the *emotions* and peripheral reflexes to *produce* their natural *effect upon* the *vasomotor system*, how much more simple and satisfactory would the investigation of asthma become." Gayford[345] takes the view that asthma frequently arises as a reflex from cardiac disease causing contraction of the muscle fibers of the finest bronchi.

Watson-Williams[346] writes, "It would appear that just as the alæ nasi above, and lower down the vocal cords, contract and dilate with expiration and inspiration, so still lower do the bronchioles. Thus air inspired through the open nostrils, glottis, and bronchioles is to some extent locked in the alveoli; hence inspiration is prolonged as compared with expiration. Now in asthma this physiological rhythmical contraction and dilation of the bronchioles is exaggerated by the increased stimulation of the corresponding bulbar nuclei; hence expiration is more prolonged and more and more air is locked in the alveoli because the expiration is so prolonged that the patient has to take in a fresh breath before the last inspired air has been expired." *He raises objection to the turgescence theory in that the swelling of the bronchial mucosa must cause as much obstruction to the entrance as to the exit of air through the narrowed lumen.* The above theory was first suggested some years earlier than this reference indicates.

Hare[347] says his theory is briefly stated as follows: "There is a widespread peripheral vasoconstriction, just as occurs in the disorder known as vasomotor angina pectoris and in migraine. Simultaneously, or practically so, there is *vasodilation in the bronchial—not the pulmonary—area.* This vasodilation must limit the rise in the general or aortic blood pressure which tends to follow the peripheral vasoconstriction; hence it may be regarded and spoken of as compensatory. As a combined result of the two opposite vascular changes, there may be a rise of general blood pressure, but there is necessarily a *sharp localized rise of blood* *pressure in the bronchiolar mucosa leading to engorgement and swelling. This swelling constitutes the obstruction characteristic of clinical asthma.*"

Auld,[348] speaking of asthma in cardiac disease, says, "Are the asthmatic attacks in these and similar instances intrinsically due to the reflex action, or are they merely provoked by it? *So long as the cause of asthma is unknown, so long will uncertainty and confusion prevail.*" Campbell[349] thinks asthma results from narrowing of the smaller bronchi, and although he admits muscle spasm cannot be positively eliminated, he is inclined to accept *turgescence* as being the *essential factor.* As proof he cites a case of *hay fever asthma* that *had the sensation during the attack of an extension of the process throughout the bronchi.*

Lugo-Viña[350] believes there may be some connection between asthma and conception, as he found two patients who had had periods of several years each in which they had asthma and no pregnancy, while one case had two children before the asthma period and five afterward. The other patient bore children after the asthma was relieved. *The attack in one came on following a severe catarrhal bronchopulmonary affection, and in the second, followed fright.*

Cott[351] says, "I believe it is simply a toxemia and that these other conditions, such as bronchitis, etc., are concomitant and not the causes or effects." Solis-Cohen[352] found two cases of dyspnea apparently paroxysmal and simulating *asthma* which *resulted from aortic aneurysm.* They had wheezing, sonorous, and sibilant râles and paroxysms in which the dyspnea was worse than at other times. The onset of each case was sudden.

Lewis[353] says, "Keeping in mind the idea that bronchial asthma may be largely an anaphylactic reaction, we find it less difficult to explain the discrepancies between cases of pronounced asthma showing slight or undemonstrable nasal disease and those showing very extensive nasal disease with little or no asthma." McDonald[354] thinks that idiopathic asthma can be cleared up by a study of the food, drink, adenoids, tonsils, alimentary tract, etc.

Matthews[355] is of the opinion that anaphylaxis plays the important etiologic role in *asthma,* and that the source of the protein may be *from* the bacteria of a *bronchitis* or *bronchiectasis.* Koessler[356] says, "In most cases of bronchial asthma the causative factor lies in an allergic reactibility of the individual. The multiplicity of asthmatogenous substances is explained by the multiplicity of anaphylatoxins.''

Ssokolow[357] writes, ''Although often difficult to differentiate, cases of pure thymic asthma occur; it is characterized chiefly by dyspnea during expiration.'' He believes the sudden deaths often attributed to the thymus cannot be from the pressure of the gland; he does not attempt to say whether the pressure causes the dyspnea or not. Edelmann and Karpel[358] found that during an attack of asthma the urine became cloudy with leucocytes, a large percentage of which were eosinophiles. They suggest that asthma is not a disease of the bronchi but is general.

Denker and Brünings[359] say there is a *catarrhal type* as well as the neurotic type. Freudenthal[360] says in regard to the appearance of the *bronchial mucosa,* ''it *will be found more or less swollen, often to such a degree that the cartilaginous rings cannot be seen at all. This swelling is sometimes so pronounced that it bulges into the lumen of the tube and for a moment one may be in doubt whether one is in the trachea or esophagus.* . . . . *In the smaller bronchi this condition is even more pronounced, so much so that occasionally, as has been pointed out before, the orifice of a smaller bronchus does not appear larger than the head of a small pin.''*

Ephraim[361] *observed* through the bronchoscope that *an application of adrenalin to the bronchial mucosa of* an asthmatic *reduced the redness and swelling;* he thinks that *hyperemic swelling and hypersecretion play an important causative part.* The *intrabronchial administration* of the drug was much *more effective* than any other method in *reducing the redness and swelling, and the effect was more lasting.*

Minkowski[362] states that *hindering the exit of air by coughing increases the intraalveolar air pressure and that this in turn interferes with the circulation of the blood through the lungs,* but gives no details of his conception. Adams[363] takes the view that *asthma* is primarily *due to errors* in diet *which congest the mucosa of the respiratory tract.* He thinks *he has, through the bronchoscope, observed congestion.* He says adrenalin may do good by stimulating the right heart.

Sachs[364] believes that some asthmatics are subjects of an exudative diathesis and vagotonia, and for this reason are unusually susceptible to anaphylaxis which directly produces bronchial muscle spasm. Gouget[365] upholds anaphylaxis as explaining asthma. Wagner[366] had two adults who were given immunizing doses of diphtheria antitoxin. Both developed in about 10 hours *paroxysmal sneezing lasting one to two hours, followed by acute asthma.* McClanahan[367] says, "In infants and children there is *usually* some *congestion of vasomotor origin or an acute inflammation of the respiratory tract.*" Of 20 cases in his series, *all* but one *gave evidence of inflammation of the bronchi preceding asthma.* Landouzy[368] advances the theory that *asthma* may occur as an anaphylactic reaction to *tubercle bacilli.*

Brown[369] treated a severe asthmatic by means of hypnosis. She had permanent relief. He argues "muscular bronchiolar contraction being relieved at once by indirect subliminal suggestion is the chief factor in the creation of asthma." Goldmann[370] *cured cases by removing infected tonsils, bad teeth, and other foci of infection about the mouth; and advanced the theory that these infective processes extended to the mucosa of the bronchi and were responsible for asthma* in this way.

Chelmonski[371] reports 13 cases of *asthma* in which he found *enlarged peribronchial lymph glands.* He says the more severe the symptoms, the larger were the glands. He offers the suggestion that such glands are a primary factor in asthma and that a resulting disorder in their internal secretion comparable to what occurs in the thyroid in Basedow's disease is secondarily responsible.

Debidour[372] in a discussion on the treatment of asthma with mineral waters asserts that an important factor is the neuroarthritic diathesis and that hence elimination is of great value as a therapeutic procedure. Hoffmann[373] takes the view that the morbid changes in asthma are in the medulla oblongata and are comparable to the changes in the brains of epileptics. Flurin[374] says an intoxication of variable origin—as from disordered nutrition, deranged internal secretions, abnormal kidneys, and fermentative changes in the gastrointestinal tract, etc.—directly affects the centers in such a manner as to produce the attacks; he calls attention to the fact that *tuberculosis and asthma* are now being considered somewhat *interdependent;* he believes that the *bronchitis commonly found with asthma* is a result rather than a cause.

Eustis[375] supports the theory that bronchial asthma results from intestinal toxins. He claims to have knowledge of 121 cases of spasmodic bronchial asthma "which were associated with an intestinal toxemia and were relieved by relieving this latter condition." Eustis concludes that there is some muscarin-like body in the toxin taken up from the intestines by the blood.

Lévi[376] takes the view (1) that the endocrinous glands, particularly the thyroid, by a disturbed secretion may produce a general condition—a so-called neuroarthritic diathesis—which may predispose to *asthma* and (2) that the *respiratory tract* may be *affected* in several ways, directly or reflexly, *to disturb* the muscle, *the vessels or the secretions of the bronchi.* He says the administration of thyroid extract in certain cases is of great value and reports the cure of twenty by the use of it.

Cholewa[377] offers the explanation that in asthma an irritable nervous system exists—especially a vagotonia—and that stimuli, psychical and physical, are reflected to the abdominal region in such a way as to cause constriction of the blood vessels, *driving* the *blood and lymph* from there *to the chest* and skin; *the lung vessels are soon overfilled* (he holds they have no vasoconstrictors); the liver and kidneys consequently functionate improperly; the *heart* has to work with an oversupply of blood; the left develops *insufficiency* and soon afterwards the *right.* From these come changes in the alveolar tissue which lead to diapedesis of leucocytes into the lumen of the alveoli and *active secretion from the glands of the mucosa, all of which make respiration, especially expiration, labored.*

Curschmann[378] reports two cases of Basedow's disease that also suffered from asthma. He tends toward the view that asthma may result from either a vagotonia or a sympatheticotonia, both of which may be manifestations of Basedow's disease. Posselt[379] takes the view that *nasal pathology* is *common in asthmatics,* but is not always guilty of causing the attacks and hence need not always be relieved.

Siegel[380] considers *asthma* a reflex neurosis, with its *pathology in* the respiratory center, the bronchial muscle, or *mucosa.* Bonnier[381] reports the cure of 75 of 100 cases by cauterization of sensitive spots in the nose. He *selects those spots which, when touched, most readily cause sneezing, lachrymation, etc.* Staehelin and Schütze[382] by spirometer experiments found that the ventilation of the lungs in asthmatics was equally good if not better than in normal individuals. They call attention to the *subjective factor which naturally arises from slightly distressed breathing and which causes a greater effort to be applied to* both inspiration and *expiration.*

Teixeira[383] reports two cases in which the *asthma* was apparently *due to syphilis,* as treatment for the latter cured both conditions. Manoiloff,[384] to obtain further evidence that anaphylaxis plays a part, sensitized guinea pigs to serums of asthmatics and of nonasthmatics. Later he injected the guinea pigs with solutions of Charcot Leyden crystals. The pigs receiving nonasthmatic serum gave no reaction, while those that had asthmatic serum showed slight reactions which, it was concluded, were anaphylactic in character.

Saenger[385] holds that *previous to asthma* there is *catarrh of the respiratory passages which produces congestion and secretion.* In a considerable number of these cases, however, he says *no history of bronchitis is* obtainable, but that this is *not evidence that a previous bronchitis has not existed,* as *patients are prone to forget mild attacks of "cold" or grip and are very certain to have firm recollection of a dyspnea attack.* He thinks asthmatics have definite physical anomalies, not always the same for every case, but that each has also a *psychic factor* which is more or less constant. The *individual attacks are excited by a morbid attention to respiration, exertion, sneezing, coughing, disturbances of digestion, menstruation, certain odors, etc.*

Jackson[386] ventures the opinion that the adrenal secretion has for one of its functions the counteracting of bronchial constriction whenever there may be a tendency for constriction from pathologic processes or products.

The following is quoted from Osler:[387] *"The hyperemia and swelling of the mucosa and the extremely viscid, tenacious mucus explain well the hindrance to inspiration and expiration and also the quality of râles."* Weiss[388] believes that an accumulation of carbon dioxide has its effect upon the central nervous system in such a manner as to produce the paroxysms. The cause of the of the walls of the bronchioles. Quoting, "Secondarily *congestive swelling with exudation into the bronchial cavity occurs in many cases* and the spasm of the bronchial wall is probably aggravated by the distention of the *distal air sacs pressing upon and further constricting the bronchioles.*"

Large[404] believes that asthma results from an irritation of the respiratory center coming reflexly from a morbid condition in some distant organ. He refers to *nasal, pharyngolaryngeal, bronchial,* intoxication, and neurasthenic *asthma.*

Cloetta[405] obtained in animals a type of dyspnea which very closely simulated the dyspnea in man known as asthma. He found an increase in the volume of air expired, and consequently an increase in the work of expiration with ventilation kept at a normal level. This, he says, is caused by muscle spasm, and not by a lack of elasticity of the lung tissues. He thinks that the dyspnea results (1) from the unaccustomed work that has to be done, and hence is done uneconomically; (2) from the *increased volume of the lungs causing pressure upon and stretching of the blood vessels, and secondarily an increased work for the right ventricle;* and (3) from the subjective sensation arising from the force of inspiration and expiration applied to the chest. Cloetta thinks the increased pulmonic pressure apparently does not have any effect upon the work of the heart because of the direct pressure, but that the *right ventricle must hypertrophy in long continued asthma.*

Casselberry[406] believes that *asthma and nasal sinus disease are closely related,* not as cause and effect, but as resultants of the same systemic dyscrasia. He has repeatedly observed in these subjects a "rapid formation of an edematous or polypoid exudate so profuse as to seem entirely disproportionate to the local cause, traumatic or other nasal irritation, unless it were promoted by systemic conditions." He goes on to say that after removal of the polyps the patient is often greatly bothered with the accumulation of these translucent exudates.

Matthews[407] says in a series of 300 cases of asthma, 90 per cent had *lesions in the upper respiratory passages, "chronic suppuration,* or the retention of mucoid secretions in *the nose or accessory sinuses.*" He further says, "The relief of asthma by any known treatment does not mean that the patient is permanently cured, since the susceptibility remains through life, and signs and symptoms will recur whenever there exist conditions favorable to the production and absorption of the specific antigen to which the individual is sensitive. Until a safe and efficient *method of desensitization* is possible the *treatment of asthma* must be directed, as in the past, to the relief of symptoms by whatever measures are indicated in each individual case.''

Leroy[408] explains asthma on the basis that the osmotic tension of the blood, becoming greatly increased through the presence of peptone, albumin, amino acid, etc., *disturbs the circulation in the lungs.* He advises blood letting. Glasgow[409] reports a case of asthma which developed *syphilis,* for which salvarsan was given. The *treatment relieved* for six months at least *the* spasms of *asthma* which the man had had since infancy.

Wolf[410] accepts the muscle spasm theory. Latham[411] reports one *case* that was *cured by the removal of a parrot from the house and another by changing his residence from the neighborhood of a chemical manure factory.* Calwell[412] says, ''*You seldom get a case of chronic bronchitis without emphysema and there is, also, not infrequently, an asthmatic element,* sometimes more marked, sometimes less.'' He also speaks of the *strain on the right heart* from the *emphysema,* and says dilatation is likely.

Ephraim[413] calls attention to the fact that a *bronchiolar muscle spasm* produced in animals by stimulation of the vagi *does not produce* the *typical breathing of asthma.* He also says it has *never been proved* in man *that stimulation of a nerve or of the respiratory center can call forth asthma.* Ephraim found that during the free period an endobronchial injection of adrenalin in asthmatics liberated an *excretion* which *yielded desquamated bronchial epithelium, spirals,* etc. This he took as *evidence of* a mild chronic *inflammatory process.* He says *coughing, laughing, crying,* and other *psychic disturbances, plus the filling of the blood vessels* by the horizontal position, filling of the stomach, etc., is likely to *cause plugging of the smaller bronchi.* When this becomes sufficiently extensive, a *spastic reaction akin to spasm occurs.*

Smith[414] takes the view that the nervous system is primarily at fault in asthma. Grant[415] thinks that many cases depend upon some *pathology of the nose* and advises persistent treatment of the nose even though results do not promptly follow. He thinks the treatment given the nose is often too superficial. Grünwald[416] says the *essential factor in asthma is dry bronchitis often unobserved.* Dick and Burmeister[417] injected emulsions of triturated tonsils into animals and came to the conclusion that asthma and other spasmodic conditions might result from the toxins of tonsillar tissue.

Kassowitz[418] reports that his findings confirm those of Lederer in regard to the occurrence in rachitic children of a condition of the smooth muscle tissue, which they designate "spasmophilen diathesis." When it is the bronchial muscle that is affected, asthma results. Goldschmidt[419] is of the opinion that the diagnosis of *asthma* is frequently confused with that of *bronchitis* and that it should never be made without the *characteristic sputum findings.*

Gage[420] advances a rather unusual theory. He says that *asthma results "because of* a lessened or of an overabundant *blood supply* to the lungs together with an inability on the part of the lung tissue to properly eliminate certain toxic products due to previous faulty metabolism." He holds that if the pulmonary vessels are greatly dilated, the alveoli are so compressed as to afford an insufficient supply of oxygen to the blood; whereas if the vessels are constricted, too little blood gets through the lungs to carry oxygen to the tissues.

Patton[421] holds there is *always* some *alteration of the mucosa of the bronchi and* that the *chief therapeutic consideration is the bronchial catarrh.* Stäubli[422] says the *psychic factor* is *of great importance* and that the *pathology* lies in the bronchial muscle or *in vasosecretory changes of the mucosa.* He advises a *journey* to the mountains, adrenalin, atropin, *and psychic diversion.* He concludes an exhaustive article on asthma by saying that on the basis of an inherited constitutional tendency to disease, the asthmatic develops especially a heightened irritability of the bronchial musculature and mucosa innervation, and the process of breathing is in close connection through the nerve centers with different kinds of influences reflected from the respiratory tract, the gastrointestinal canal, the genitals, the skin, climatic factors, fear, and other psychic excitants. In this way the bronchial musculature may be thrown into spasm and the *mucosa* stimulated to *secreting,* and thereby the *ventilation* of the alveoli will become *dif-*

*ficult.* Stäubli says there is *also a cardiac, a psychic or hysteric, and a uremic asthma.*

Glück[423] expressed the view that when inhalations and smokings give relief, the attack has advanced only to the stage of spasm of the bronchial muscles and that it might go on to *swelling of the mucosa* when more energetic means are required. Patton[424] emphasizes the importance of reflex causes of asthma by reporting a case which he *cured by the removal of buried tonsils.* He says "nothing abnormal was found save *emphysema* and *buried tonsils and* that *touching the tonsils* on two successive days *brought on* each time a *violent attack of coughing and sneezing* lasting 20 minutes or more." Quoting further, "It is generally accepted that bronchial asthma is a neurotic affection characterized by *hyperemia and turgescence of the mucosa of the small bronchial tubes and a peculiar exudate of mucin."* Patton goes on to say that the attack may be due to reflex stimulation originating in the respiratory tract or any other part of the body. He holds that the nose is commonly responsible.

Hofbauer[425] says his experience early led him to the conclusion that *asthma* is not the cause, but the *result of bronchitis,* that *emphysema develops concurrently,* and that there must be *some connection between asthma and the lung changes.* He has devised an apparatus known as an expirator. By this he *regulates the time of each phase of respiration.*

He claims the following: (1) the patient's *mouth is closed during the entire respiration cycle and hence coughing, sensation of pressure on the chest, and other harmful results of an open mouth are avoided;* (2) *attention* is withdrawn from inspiration and centered *on expiration;* and (3) the *patient learns to gradually increase the expiratory phase and not to apply muscle force to it. Seven years' use of the method has proved its value. Many cases* in which other therapy has failed have been *benefited.* Hofbauer explains his good results on the theory advanced by Löwy that stretching of the alveoli causes stretching and stimulation of the vagi endings. His method tends to minimize this effect, he thinks.

Grossmann[426] found that stimulation of the *nasal mucosa caused lung congestion.* Kayser[427] worked on rabbits and concluded that the theory of bronchial muscle spasm probably explains asthma. Shambaugh[428] reports a mild *asthma* which *followed* the *eating of* *grape fruit.* He says, "Her *eyes would swell shut and the edema would extend to the conjunctivæ and was associated with* some *sneezing.*" Adam[429] is firmly convinced that asthma depends upon imperfect protein metabolism from insufficient exercise and excess of carbohydrate in the diet.

Krez[430] says *in* his experience with *2000 cases of asthma* that in addition to a neurotic element in each case there was *always* more or less *catarrhal condition of the bronchi.* He says that in some cases there is five per cent catarrh and 95 per cent nervousness and in others the proportion is reversed, and that there are, of course, all grades between. He writes, "When we ask ourselves the question, from what comes the *catarrhal disposition* I give the answer, *from tuberculosis.*" In his series of cases he reports that at least 75 per cent gave evidence of *apical involvement with tuberculosis.* His *histories* very commonly *give* further *evidence of a previous active stage of the disease* and he records *instances of intimate association with consumptives and much family tuberculosis.* He says as *asthma* is relatively *common with latent tuberculosis,* it is relatively rare in acute tuberculosis. He saw one case with lung bleeding and asthma and concludes the *asthmatic must be treated as* a neurotic *tuberculous individual and given abundance of rest, fresh air, and good food.* He advises the *selection of a suitable climate.*

Winter[431] is of the opinion that the paroxysm results from vagus irritation which in turn causes a *dilatation of the pulmonic vessels.* Hutinel[432] says *asthma* in children is usually the *result of a catarrhal process* in *the upper respiratory passages,* commonly *causing enlarged bronchial glands, and* that the *removal of the adenoids and tonsils benefits a certain percentage of cases.*

Francis[433] holds that *asthma results from vasomotor disturbances* caused by unstable blood pressure. He claims the galvano-cautery to the nasal mucosa stabilizes the blood pressure and, therefore, benefits asthma. Hajek[434] says it has long been known that the *nose* may be *connected in some way with* the cause of *asthma and* that *operations on the nose may effect a cure,* but he says he has seen cases in which asthma was cured or was caused to disappear by other trauma, as for instance the breaking of bones.

Tauszk[435] claims to have found a type of *tuberculosis* which is particularly *prone to become asthmatic.* He says the *diagnosis of pulmonary phthisis is frequently very difficult* to make and that with it there is *commonly a well marked bronchial catarrh and the asthmatic type of breathing.*

Weber[436] reports an elaborate piece of work on experimental asthma. He used a large number of animals, producing marked asthma by the use of imido-Roche or muscarin and a weaker asthma with digitalin, with barium chloride and with peptone. To relieve the asthma, he made use of adrenalin, nicotin, atropin and nitroglycerin. He took tracings from lobes of lungs which were moving, from some which were quiet, and from others severed from the central nervous system, all the while measuring the tracheal pressure. This was done both with and without artificial breathing.

He says that by binding a tube into the large bronchus of a lobe of the lung, the respiration can be kept up artificially the same as in the remainder of the lung. The nerves to these lobes can be interrupted while those to the other lobe need not be disturbed. By means, then, of oncometer tracings the volumes of two lobes, one of which may be isolated from the central nervous system, can be registered. In this condition the introduction of the muscarin group brings about contraction of the bronchial muscle only in that lobe in which the nerves are intact.

The effect of the imido is very greatly lessened in the lobe disconnected from the nervous system. From this he arrives at the conclusion that to a great extent the action of the agent which produces asthma is not peripheral, as heretofore assumed, but central. In animals with the chest opened, even though there is a greater contraction of the bronchial muscle, the lungs do not become distended, while artificial respiration causes distention even though there is contraction of the bronchial muscle. This leads Weber to say that the *distention seems to result because the expiration strength is less than that for inspiration.*

The author found that the drugs which affected the bronchial muscle also and in a similar manner affected the blood vessels. He therefore asked the question—and attempted to solve it—whether a filling of the lungs with blood would to any degree interfere with the introduction of normal amounts of air into the lungs and thus lead to asthma.

If the *chest* was *open*, the *greatest filling of the vessels of the lungs had no effect upon the amount of air accommodated.* In an animal in which all possibility of contraction of the bronchial muscle fibers had been eliminated first, with chest intact, and afterwards with it opened, imido was introduced into the blood. *With the chest intact, marked asthmatic breathing was produced, but with the thorax open only a marked filling of the blood vessels of the lungs occurred.* From this he concluded that *asthma may result purely and solely from filling of the pulmonary vessels.*

Roth[437] takes the view that when nasal stimuli cause asthmatic attacks, there must first exist an unstable, easily stimulable nervous system. Pal[438] says the mere fact that an attack is relieved by putting cocain and adrenalin in the nose does not prove the nose to be the cause, for the drugs are absorbed and exert a systemic effect; but he has found with the same drugs given hypodermatically relief comes in 20 to 30 minutes, whereas when applied locally to the nose, relief comes in three minutes. This, he thinks, proves that a part is played by the nose.

Baar[439] made a study of asthma in relation to barometric pressure and found that the time of low readings is when cases are most likely to be sent to the hospital. That is, he thought attacks came with or because of low barometric pressure. The author offers in explanation of this phenomenon the suggestion that radioactive emanations may be freed from the earth at low pressure and produce *vasomotor changes* which are *responsible for asthma.* The rising barometer, he suggests, may have a vagus stimulating effect—one which tends to do away with vasomotor changes.

Missildine[440] reports *"horse" asthma characterized by rhinitis, pharyngitis, and laryngitis.* He found that these patients reacted with itching and other manifestations of anaphylaxis to horse serum of a dilution of 1 to 700 dropped into the eye. An abrasion of the arm developed edema and redness after an application of a 1 to 10 dilution of the serum. In one case he sprayed a very *small amount of the diluted serum on the Schneiderian membrane* and *produced a "paroxysm of violent sneezing* which lasted 10 minutes and was *followed with a typical asthmatic attack."*

Widal, Lermoyez, Abrami, and Brissaud[441] conceived the idea that further proof of the relation of asthma to anaphylaxis could be obtained by a study of the blood and blood vessels in both conditions. In anaphylaxis they found a leucopenia, a fall of arterial tension, a hypercoagulability of the blood and a diminution of the refractive index of the serum. They concluded that asthma is the result of some serious physiochemical phenomenon of the body fluids and may properly be compared with paroxysmal hemoglobinuria and the crises of the alimentary urticaria. They take the view that the dyspnea is only an apparent, a minor and objective symptom of the more profound changes.

Davies[442] states, "The occurrence is paroxysmal and painless, stamping it at once as a neurosis. It is characterized by spasm of the bronchi and the respiratory muscles, including also the diaphragm, and is followed by a *vasomotor disturbance in the mucous membrane of the bronchi,* large and small. The nearest answer yet afforded is that it is a reflex from an irritation produced elsewhere in the body." He reports cases illustrating seven types of reflexes and says that appropriate operations afforded relief—in most cases, complete. The types he reports are as follows: dysmenorrhea, retroversion and adhesions of uterus, undescended encysted testicle, indigestion (lavage gave relief), adenoids and large tonsils.

Rohmer[443] reported asthma occurring in a six year old child three days before death; the child had mitral insufficiency with tremendous dilatation and hypertrophy, and the autopsy revealed the characteristic findings of asthma in the lungs. He calls the condition cardiac asthma. Goodale[444] tested five cases of "horse" asthma by applying horse serum to an abraded surface of the skin, causing a sharp localized edema and reddening in each. In three of the cases when the serum was applied to the *nasal mucosa, edema, watery discharge and sneezing* occurred.

Joppich[445] expatiates on the necessity of combating the predisposing factors in asthma, studying whether the over sensitive nerves belong to the peripheral or central nervous system and the influence of *overwork* and *worry,* of *dust, soot, fogs, or odors,* acting directly or by summoning up memories. The reflex irritation, he says, may be set up from the digestive, respiratory, genital organs, or the skin, and each case must be analyzed to discover and remove the special exciting factor. Keiper[446] observed *in an asthmatic* that "the *mucosa was much congested and swollen.* When the second bifurcation was reached we could see *rhythmic contractions* taking place *in the bronchus* almost closing it."

Abbott[447] in a very comprehensive though succinct article says, "Granting asthma as being caused by anaphylaxis, at least a very large percentage of cases have a nervous origin." He blames ethmoiditis for most of the cases, but considers *bronchitis a dangerous accompaniment.* In emphasizing the part that the nose plays he says, "The *cough* will improve just as fast and no faster than the improvement in the *ethmoiditis.*" He goes on to say that this class of cases usually *complains most of severe "colds"* in the head *and* is *subject to coughing spells, especially between midnight and four o'clock in the morning. He sees no reason, however, for the absence of asthmatic symptoms in those cases of nasal trouble that do not have asthmatic attacks.*

Mayer[448] found that nine of 40 cases of *chronic bronchitis and asthma* failed to eliminate uric acid from the blood with the same rapidity as a normal individual eliminates it. In these cases there was usually a family history of gout and diabetes and the children almost invariably showed the exudative diathesis. *Treatment of* the patients for the *gouty condition* greatly *benefited* their *asthma.* Jepsen[449] found *in all his cases vasomotor rhinitis,* which fact, he thinks, suggests the importance of a reflex factor in asthma.

McPhedran[450] writes, "Pathologically *the affection is characterized* by a spasm of the bronchi and of the respiratory muscles including the diaphragm, and *by vasomotor disturbances of the bronchial mucous membrane. . . . . Disease of the respiratory mucous membrane, especially catarrhal conditions of the nasal passages are of frequent occurrence before the development of asthma. . . . . All chronic cases show various secondary changes of which bronchitis and emphysema are the most frequent.*" He says *the fact that asthma-like dyspnea occurs in certain cases of capillary bronchitis proves the swelling of the mucosa is at least capable of inducing the paroxysms; the secretion also suggests congestion* of which the white spirals present in many cases are the product.

Dudley[451] says, "In the study of the nasal conditions acting as exciting causes of asthma and their relation to the prognosis and treatment of the same, we must not overlook the one large factor in these cases; namely, a cerebral condition, inherited or otherwise, acting against the inhibiting influence of the brain in the normal individual, which allows a reflex to be transmitted to the bronchi, resulting in a constriction of its circular fibers, resulting in the distressing dyspnea so familiar in these cases. It seems to the writer also that *in the pathology of the cases depending upon diseases of the sinuses,* in many of the cases pressure upon sensitive nerve endings of the fifth and other nerves cannot be accused of exciting the reflex, but *we must look for some other connecting link* which anaphylaxis appears to fit better than any other hypothesis at the present time."

Weltey[452] says, "The same nasal conditions that produce asthma also produce neuralgia, headache, hay fever, etc." He estimates that 60 per cent are due to the nose, 20 per cent to poisons and toxemias, and about 20 per cent to purely medical conditions.

Talbot[453] reports six cases of *asthma* in children in which the *etiologic factor* seemed to be *egg white poisoning.* In every case a skin test proved sensitization to egg albumen, and its administration usually, even in therapeutic dosage, seemed to aggravate if not directly cause attacks. *Immunization* to the albumen *brought* about a *cure or great improvement* of the asthma. Talbot concludes that asthma is a manifestation of anaphylaxis; i. e., its local manifestation in the lungs. He concedes that *urticarial eruptions* may come *upon the mucous surface of the bronchi.* He thinks *many other than egg or horse protein may be etiologic factors.* Plesmann[454] holds that *catarrh of the air passages* is the *most important factor in asthma.*

In May, 1914, I[455] made the following report to the Missouri State Medical Association: "The sequence of events that are responsible for an attack of bronchial asthma, according to my view is about as follows: (1) *the patient has a bronchitis* more or less of a chronic nature; (2) he *coughs* considerably—*in paroxysms* at times; (3) the forceful *coughing causes a damming of the blood into and back of the right heart;* (4) *this increased venous pressure causes an increased pressure in the bronchial vein and in the bronchial capillaries;* (5) as the venous pressure increases, the *flow of lymph* from the thoracic duct and its tributaries will also be more or less *hindered;* (6) the *damming back of the lymph into the lymph spaces of the bronchial mucosa and of the blood into the capillaries of the bronchial vein causes a swelling of the mucosa* *of the bronchi;* (7) *in the smaller bronchi this swelling is sufficient to greatly obstruct the passage of air through the bronchi;* (8) *during inspiration the damming back of blood and lymph is decreased and air is allowed to pass through the bronchi more readily than during expiration.*

(9) *As the expiratory effort forcefully dams back the blood and lymph, the expiration becomes very difficult;* (10) *there is thus established a vicious circle,* particularly if there is any coughing after the dyspnea develops; (11) the morphin and strychnin relieve the attacks by virtue of the facts, I think, that the *morphin relieves the bronchial irritation and* some of the *mental anxiety* while the *strychnin probably does its work by its effect on the arterioles,* raising the systemic blood pressure and *increasing the nourishment to the overworked right heart.*"

Hertoghe[456] says, "There is no doubt that many asthmatics are the subjects of thyroid insufficiency. Unexpected cures in asthma as the result of thyroid medication have been described by several authors." Hoover and Taylor[457] think the real difficulty of ventilation in emphysema and asthma lies in the distention of the infundibula; this fails to allow an equal diffusion of carbon dioxide throughout the alveolar air. They say, "Asthmatic patients usually develop cyanosis with a lower carbon dioxide pressure in the alveoli than do nonemphysematous or nonasthmatic patients."

Lewis and Barcroft[458] report a series of cases in which reduced alkalinity of the blood, usually plus *cardiorenal disease* of varied grade was found to be the *cause of dyspnea.* They say, "We consider it highly desirable that *attention* should be directed *to all forms of paroxysmal dyspnea from the standpoint of blood reaction during the attacks.* It seems possible, if not probable, that *many instances of spasmodic dyspnea may result from a similar causation.*" Ullman[459] holds that asthma is from endogenous or exogenous proteins.

Haddon[460] takes the view that the skin is the organ primarily at fault, and when once it eliminates normally the asthma will cease. He advises the proper regulation of the diet. Koessler and Moody[461] say, "We hold that *in most cases of true bronchial asthma the causative factor of the disease lies directly in the bronchi, that the concomitant focal infection and the bronchitis caused by it constitute the primary condition* and that the asthmatic patient has become sensitized or anaphylactic to the *infective agent causing* his *'cold' and* his *bronchitis.*"

Babcock[462] agrees with Koessler and Moody that asthma is a phenomenon of anaphylaxis and that sensitizing protein comes from the *bacteria of a bronchitis,* but he holds that the *bronchitis is not always primary.* He offers as an example of this a case that had an *abscess at the tip of a tooth. Extraction of the tooth with cure of the abscess gave much relief and vaccines from the bronchial exudate completed the cure.*

Lord[463] believes asthma "an independent affection, unconnected with obvious disease of the heart, the lungs, or other organs," characterized by paroxysms of dyspnea affecting both inspiration and expiration. He says that *cough* and the expulsion of *tenacious sputum* follow the attack and after a time *chronic bronchitis and emphysema* result. He believes *bronchial spasm does not satisfactorily explain the attack* and very significantly states that the so-called *neuropathic constitution may well be regarded as a result instead of a cause of asthma.*

Mayer[464] reports upon his studies of 40 cases of *chronic bronchial catarrh or asthma—or both*—and repeats his earlier conclusions that in some cases at least, there is a chain of conditions at the time of the exacerbation of the bronchial affections the same as in recognized gouty states. The curve for the elimination of uric acid in the latter was simulated by the former. He holds there is little doubt that there is a connection between the "lung gout" and exudative diathesis.

Zueblin[465] reports two cases, both of which gave *positive histories of "colds" and coughs* of variable duration *preceding the paroxysms.* He is inclined to blame a hypersensitiveness of the posterior lobe of the hypophysis for asthma. He thinks this may be *caused by an irritation of the bronchial mucosa.*

Sajous[466] defines asthma as "a neurosis characterized by more or less severe paroxysmal dyspnea, due to spasmodic narrowing of the bronchial lumen alternating with spasm of the muscles of the thorax." He holds that *catarrh of the bronchi exists* in a small percentage of the cases and that in these emphysema develops later. He refers to the developing of *tuberculosis* concomitant *with asthma.* Quoting, "I have advanced the view that the *bronchial irritation* which underlies the spasm was originally due to the presence in the blood of toxins, toxic wastes, etc., which are *eliminated by the bronchial mucosa* in addition to their morbid influence in the central nervous system."

Shivdas[467] has observed that *bronchitis and asthma* seem to *have connection* in some cases *with pyorrhea alveolaris as treatment for the bronchitis alone is not so effective as when combined with treatment of the pyorrhea. The improvement in the asthma is in direct proportion to that obtained in the pyorrhea.*

Oftedal[468] writes, "It seems evident that the *sputum* of at least a large number of persons suffering *from bronchial asthma contains organisms* (streptococci) which have an elective affinity for the bronchial musculature and that the invasion of the lungs by these organisms, when made possible by any factor, psychic or otherwise, which tends to lower the resistance of the individual, will bring about a tonic spasm of the muscles of the bronchioles and cause the typical phenomena so commonly observed clinically in patients suffering with an attack of asthma. In other words, these experiments illustrate another example of elective localization of streptococci. There are no doubt a number of factors which must be taken into consideration. I would particularly emphasize a *hereditary predisposition to weakness of the respiratory tract. In nearly all of the cases studied, there is a family history of asthma or other respiratory tract disease.* Many of the cases give a history of spasmodic laryngitis (catarrhal croup) during childhood, which strongly suggests a congenital lack of resistance, manifesting itself as *bronchial asthma* later in life *with* the development of a *focal infection, or a weakening disease of the lungs, such as an attack of acute bronchitis.*" He gives the following history of one of his cases: "Man, aged 39, referred to me in January, had had *asthma since he was 22. Prior to that time, since the age of 14, he had coughing spells every night.* He had croup during the first year of life; when *11 years of age he was taken to a doctor to be treated for catarrh in the head.*"

Davis[469] calls especial attention to the observation that *asthma* is *common in cases of chronic bronchitis and emphysema.* Lederle[470] collected statistics on a large number of cases of *hay fever asthma* from several hundred physicians; it was found that the *average length of time for "hay" asthma to follow the seasonal development of hay fever was two weeks.*

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# CHAPTER IV.

## AN ANALYSIS OF THE HISTORICAL DATA.

An attempt to analyze and summarize the various expressions on asthma lead to but one conclusion; namely, that a theory which satisfies even a reasonable majority has not been presented.

It is an interesting and significant fact that *many* of the *writers* on the subject have themselves been *sufferers from* the *malady;* these and others have related important observations. Speaking figuratively, the brick, the mortar, the lumber, and other materials have long been accumulating and architects have not been wanting; but the satisfactory structure of an explanation has not been forthcoming.

*In considering* the *multiplicity of views on asthma,* it is necessary to hold in mind that *theoretically the respiratory function may be influenced by a large number of factors,* a few of which may be the central nervous system, peripheral nerves, intermediate centers, reflex stimuli, chest muscles, abdominal muscles, diaphragm, bronchial muscles, abnormal or alter constituents of the blood, food, medication, anaphylaxis, bacterial toxins, inflammatory areas, tumors, polyps, nose, heart, blood vessels, kidneys, lymph vessels, lymph, lymph nodes, lung tissue, physical property of the air, habit, fright, worry, etc.

Probably the many factors which might be concerned constitute the main reason why we have *not yet arrived at a satisfactory explanation* of asthma. But perhaps the fact that it has been so generally held as some mysterious nonunderstandable condition has also done much to hinder advancement in the study of the disease.

Cures result in one case when nasal polyps are removed, in a second when a gouty condition is properly treated, in a third by a withdrawal of egg from the diet, in a fourth by hypodermic administration of dead bacteria, in a fifth by suggestive therapeutics, in a sixth by blowing a mouth harp, and in a seventh by breathing exercises, etc., etc.

The *most important factor* in one case is said to be bronchitis, in a second ethmoiditis, in a third nasal polyps, in a fourth buried tonsils, in a fifth a bad heart, in a sixth some intraabdominal abnormality, in a seventh enlarged bronchial lymph nodes, and in an eighth hay fever, etc., etc.

The *difficult breathing* is due, one man thinks, to spasm of the fibers of the circular muscle of the bronchioles; while a second holds that it is from a pathologic respiratory center; a third explains it as a psychosis; a fourth believes it results from vascular change in the mucosa of the bronchi; a fifth thinks it comes from an exudative bronchitis, a part of an exudative diathesis; a sixth says it is a spasm of the diaphragm; a seventh blames the external muscles of respiration; and an eighth combines two or more of the above theories, etc., etc.

The *theory of spasm of bronchiolar muscle* has been more generally accepted than has any other, but that of vasomotor changes in the bronchial mucosa has been a close second in popularity. The cause of the bronchiolar muscle spasm, one man says, comes from some substance in the blood; while a second believes that the pneumogastric nerves or the respiratory center is wholly or in a large part responsible; a third holds that pathologic areas in various places in the body may reflexly affect the muscle; and a fourth thinks that asthmogenic foci in the mucosa of the respiratory passages may reflexly excite the muscle of the bronchi, etc., etc.

The *substance in the blood* which might affect the muscle fibers of the bronchi one man holds is uric acid; a second, some unusual unoxidized product of metabolism; a third, some toxic product absorbed from the alimentary canal, and a fourth, some protein substance to which the body has been sensitized, etc.

*To account for the condition the bronchial mucosa is supposed to be in by those who support the hyperemia or vessel turgescence theory,* it is assumed by the first that there is an urticarial swelling; by the second, that there is a loss of tone in the vessels, a so-called vasomotor paralysis; by the third, that there is a marked inflammatory swelling; by the fourth, that constriction of all abdominal vessels occurs and the vessels of the chest undergo compensatory dilatation, including those of the bronchi; by the fifth it has been hinted that increased intravesicular pressure might cause the hyperemia; by the sixth that an anaphylactic swelling occurs; by the seventh that there is an angioneurotic edema, etc., etc.

Two or three *theories* have been formulated *to explain why* the *expiration is more prolonged and difficult than* is *inspiration.* One is that the muscular power of *expiration* is *weak as compared with* that of inspiration. Another assumes that the *function of* the bronchiolar *muscles might be to expand* the *bronchioles during inspiration* so as to facilitate the entrance of air into the alveoli, *while during expiration they contract* so as to hinder the escape of the air therefrom, thus promoting absorption of oxygen; and it is therefore assumed that both of these functions are exaggerated in asthma.

*Proof of* the *muscle spasm* theory seems to have rested upon the facts, (1) that it has been conclusively demonstrated that circular *muscle fibers exist* in the bronchi; (2) that these fibers *may be caused to contract* by a stimulation of the peripheral ends of the vagi; and (3) that the muscle may be made to contract by the presence of certain substances in the blood, even when the vagi are completely out of function. This evidence can scarcely be considered sufficient, but the other theories seem to have had even less supportive evidence.

The *proof of vessel turgescence* of the bronchial mucosa seems to have rested on the fact that (1) *swelling and congestion* of the bronchial mucosa *has been observed* during attacks, passing off with the paroxysm; (2) *bronchitis commonly exists* in asthma; and (3) the *character of the excretions* suggests inflammation.

As a foundation for, or rather, *as a proof of the correctness of the ideas to be presented in later chapters, special attention is called to several observations, to-wit:*

First, in a majority of reports on asthma, mention is made of associated *bronchitis and emphysema.*

Second, in a number of instances it has been observed that during an attack of asthma the bronchial *mucosa is* markedly *edematous and reddened.*

Third, the oncometer tracings and other *experiments of Weber* showed very conclusively that changes in the circulation in the lungs are sufficient to produce asthma.

Fourth, von Strübing's students, presumably in good health, by *imitating the breathing of asthmatics* developed signs of asthma. One who became very expert found that a ''cold'' and coughing helped materially.

Fifth, not a few clinicians have observed that when *asthmatics breathe slowly and regularly,* putting no force on expiration, the attack is greatly modified and in many instances entirely checked.

Sixth, it is common observation that the attacks frequently occur while the patient is in a *horizontal position* and *after excitement* or *exertion,* and with acute attacks of bronchitis.

Seventh, morbid conditions of the *tonsils, teeth, nose, accessory sinuses* and other parts of the upper respiratory tract have been frequently noted.

Eighth, in a number of instances, cases have been described as due reflexly to the nose or the tonsils and in the splendid description of one tonsil case it was distinctly stated that *paroxysmal coughing and sneezing* immediately *followed touching the sensitive focus,* after which came the asthma.

Ninth, in *anaphylaxis asthma,* there has been observed swelling and edema of the upper respiratory tract and râles and rhonchi of the tubes.

Tenth, examinations of the *excretions from the bronchi* and of the bronchial walls at autopsy give convincing evidence of inflammation.

Eleventh, *no* very clear *explanation has been offered as to why expiration is difficult and inspiration easy* during severe attacks; it, however, has been observed that noises in the chest are more marked with forced expiration.

Twelfth, a number of clinicians have come to the conclusion that pulmonary *tuberculosis and asthma* are *often associated.*

Thirteenth, in some instances mention is made of *right heart weakness* in asthma.

Fourteenth, Heilskoy and Mahler observed repeatedly that in the attack the *bronchi nearly closed during expiration,* especially during coughing, and that after the application of adrenalin, the swelling and edema disappeared with the asthma.

Fifteenth, in hay fever *asthma* the dyspnea *does not develop with the first signs of hay fever,* but usually days or weeks or even years after the beginning of the nasal symptoms. In fact there are usually periods of bronchitis of greater or less duration in successive seasons before the asthmatic dyspnea develops.

# CHAPTER V.

## THE ESSENTIAL ANATOMY OF THE BRONCHI, LUNGS, AND HEART.

It is unnecessary to describe the *nose, mouth, pharynx, and larynx* except to say that they are richly supplied with nerves and blood vessels; and that the larynx is an oblong, cartilaginous, hollow body.

The *trachea,* a cylindrical *elastic tube* 18 to 25 mm. in diameter, is the continuation of the larynx and passes into the chest, dividing opposite the fourth or fifth thoracic vertebral body into the two bronchi. The wall consists of 16 to 20 horseshoe *curved strips of hyalin cartilage* with the openings behind. Some strips are split and united to others. The intercartilaginous spaces are occupied by *tough membranes of elastic and collagenous tissue* connecting the cartilages with each other. Some muscle is found in the walls especially in the posterior part. The mucosa of the trachea is continuous with that of the larynx and bronchi. The submucosa consists of connective tissue in which are numerous mucous glands. In the tracheal wall are also nerves and blood and lymph vessels.

Gerrish[1] describes the *bronchi* of the right lung as 15 mm. in diameter and 25 mm. in length, and the left as 10 mm. in diameter and 50 mm. in length; the right has three divisions and the left two. Spalteholz[2] says the bronchi leave the trachea at an angle less than 90 degrees and pass downward and lateralward to the hilus pulmonis; on the right the nonbranched part is steeper, shorter and wider than on the left. He writes, ''They are constructed exactly as is the trachea and have on the right side six to eight, and on the left side nine to twelve rings of cartilage which are open behind.''

The bronchi divide into numerous *branches, subdividing* finer and finer, eventually *forming the bronchioles.* The branches of the main bronchi have irregular *cartilaginous plates* distributed *about* the entire *circumference,* larger in the beginning where they are also closer together. They disappear in the tubes of 1.0 mm.

diameter, according to both Merkel[3] and Spalteholz. Gerrish states that cartilage exists in the tubes of 1.0 mm. diameter and above.

In the *bronchioles without cartilage* there is neither *glandular* nor *elastic tissue*, the *walls being* constituted of thin much *flattened*

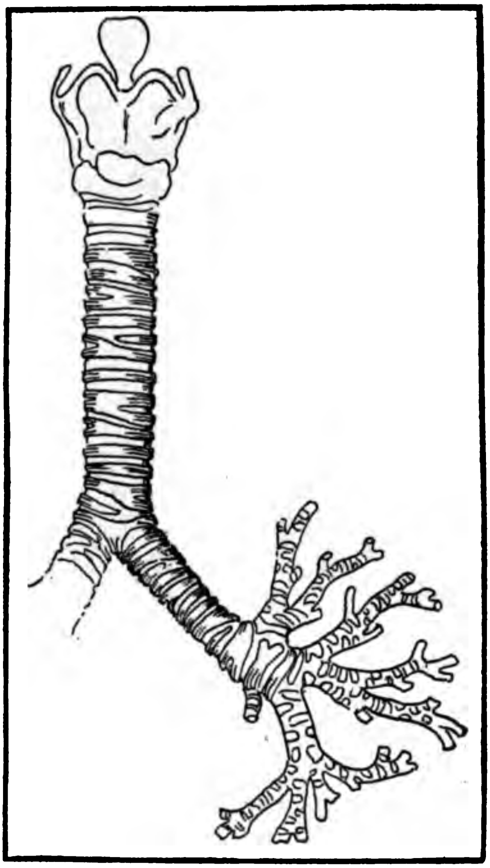

Fig. 1.—The Bronchial Tree. The walls of the bronchi contain cartilage in incomplete rings or plates distributed about their entire circumference. The cartilage and the elastic tissue make the tubes firm-walled; only the fine branches of one mm. or less in diameter have no cartilage, and are consequently collapsible.

*epithelium plus* a *thin* layer of smooth *muscle.* Aufrecht[4] found the muscular coat to consist of two layers—a relatively heavy circular coat, and a very thin longitudinal coat.

Quoting from Spalteholz, "Each *bronchiolus divides further into* *branches, bronchioli respiratorii, the walls of which are no longer smooth, but present small bulgings, alveoli.* Out of these bronchioli respiratorii, as terminal branches, pass the *alveolar ducts,* ductuli alveolares, which bear *alveoli on all sides* and *lead,* through openings in their terminal piece, *into* several approximately spherical spaces, *atria.* Each *atrium* is *connected* in turn *with* a number of larger and more *irregular* cavities, air sacs, sacculi alveolares (*infundibula*) the whole surface of which is *closely set with* small cavities, *alveoli pulmonis.* The bronchioli respiratorii and the ductuli alveolares still possess a circular layer of smooth muscle fibers but this is absent from atria and sacculi alveolares.'' The pulmonary alveoli may be spoken of as alveoli, vesicles, or air cells. (Da Costa and Spitzka.[5]) The *walls of* the *alveoli extend well into the interior of the infundibulum, or sacculi* alveolares, and the capillaries of these partitions are exposed to air in two alveoli.

We see, then, that *from each bronchiole come perhaps four respiratory bronchioles, from each of these perhaps the same number of alveolar ducts, from each of these the same number of atria, and from each of these a large number of air sacs, each of which is closely set with pulmonary alveoli.* This constitutes a *lobule.*

The *arteries* which supply the bronchi are branches usually of the thoracic aorta on the left side and of the first aortic intercostal artery, or thoracic aorta direct on the right. They follow along the bronchi and divide and subdivide, nourishing the bronchi and the cellular tissue of the lungs. The *bronchial veins return in a course relatively parallel to the arteries* gathering up the blood distributed by them and open on the right into the vena azygous major, near its termination, and on the left into the left superior intercostal or the left upper azygous vein.

According to Karstner and Ghoreyeb,[6] *capillaries of the bronchial artery anastomose freely with* those of the *pulmonary artery,* but under normal conditions the blood from the bronchial artery goes through its capillaries direct to the bronchial veins; but if the capillary pressure of the pulmonary circuit becomes lower than that of the bronchial, the flow is direct from the bronchial capillaries to the pulmonary and hence to the left heart; or the reverse may occur.

The bronchi are richly supplied with *lymph vessels* which, draining toward the hila of the lungs, empty into the thoracic duct.

*All but the finer divisions of the bronchial lymph vessels are outside the bronchi* and along their course. The lungs are incased in the air-tight thorax.

Paterson[7] says the ordinary *muscles* of inspiration are the diaphragm, intercostals, scaleni, serrati posteriores, levatores costarum, and subcostals; the extraordinary or accessory muscles are the quadratus lumborum, pectorals, serratus anterior, sternomastoid, latissimus dorsi, infrahyoid and extensors of the vertebral column; and the muscles of expiration are all the muscles of the abdominal wall and the transverse thoraces, and some say the internal interosseus.

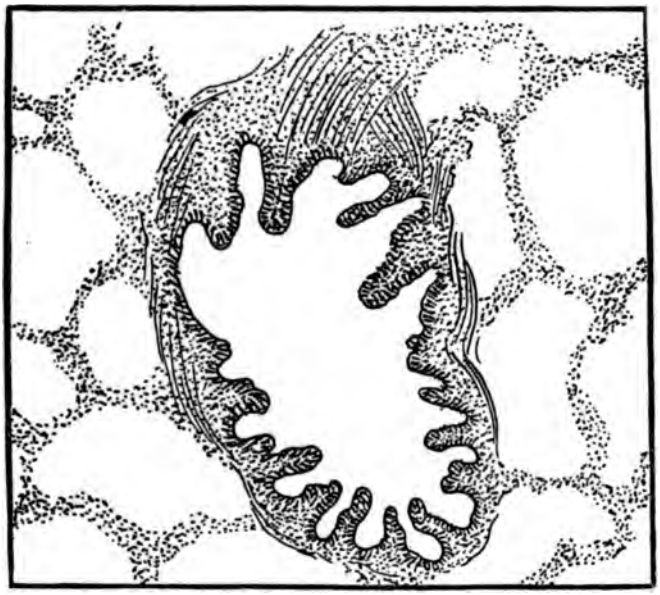

Fig. 2.—The Bronchiole. (Highly magnified.) The bronchioles are irregular tubules of a diameter of one mm. or less. The walls consist of a thin flattened epithelium plus a thin layer of nonstriated muscle. (Böhm, Davidoff, and Huber.)

Efferent *nerves* connect these muscles directly or indirectly with the respiratory center in the bulb located near and below the vasomotor center and not far from the calamus scriptorius. The vagi through the pulmonary plexes innervate the alveoli and the bronchial muscle, and through the superior and inferior laryngeals, the larynx and trachea.

The *heart* is divided into two parts, the left side of which pumps freshly oxygenated blood from the lungs to all parts of the body and the right pumps the venous blood through the pulmonary vessels. The wall of the right ventricle is 2.0 to 3.0 mm. in thickness while that of the left is 10 to 12 mm. The structures of *both divisions of the heart receive nourishment through the coronary arteries which arise from the aortic sinuses.*

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# CHAPTER VI.

## THE ESSENTIAL FACTS OF THE PHYSIOLOGY OF THE BRONCHI, LUNGS, AND HEART.

The *ventilation of* the *lungs* is accomplished by means of a variation in the thoracic space. The increase of area—inspiration—is effected by the coordinate action of various muscles named in the preceding chapter. Increase of space lowers the intrapulmonic air pressure below that of the atmosphere, and air rushes in through the trachea, equalizing the pressure.

*During inspiration* the *tissue* of the alveoli, which is chiefly elastic, *is on a tension,* and irrespective of posture, much of the weight of the structures of the chest has been raised against gravity, so that when inspiration ceases, the *chest passively falls* back *into position for the next inspiration.* Even in *normal breathing* there may be some contraction of the abdominal muscles to assist the diaphragm in its return to the position of rest, and the triangularis sterni may, in a certain measure, help in depressing the ribs, but these actions are inconsiderable. *Hence expiration* under normal tranquil breathing *is* practically *passive.* The decrease of space, however, causes an increase of the tension of the air in the alveoli.

In *forced inspiration* the muscles active in ordinary inspiration are used with greater power; these may be considerably reinforced by fixing the arms rigidly so that the pectorals *and* serratus magnus may assist in raising the ribs, thus affording fixation for the attachments of the diaphragm. In forced *expiration* all the muscles that pull downward on the ribs, as well as those that tend to increase the intraabdominal pressure, may be utilized. These include especially the very strong abdominal muscles.

*During forced inspiration there is a proportionately greater* difference between the *tension of the alveolar* and atmospheric *air* than during normal inspiration. This disproportion may be increased, even in normal breathing, by obstructions within the upper air passages, or by encroachments upon a considerable portion of the total caliber area of the bronchial tree whether formed at one point as by a polyp in the larynx or in many parts, as by secretions.

*In forced expiration, the intravesicular pressure is* proportionately *increased* over that of the atmosphere. The degree of increase depends upon the force and rapidity of the expiratory act. Here too, an obstruction in the air passages will add greatly to the pressure.

*A cough is a* sudden *forceful expiration,* usually with the mouth open and larynx sometimes partially contracted. ***Sneezing is* a** violent *forceful expiration* through the nose and the mouth. The act of ventilating the lungs is normally involuntary, but may at any time become voluntary. *The respiratory center is in control* of certain muscles *of respiration,* mainly through the phrenic and intercostal nerves to the diaphragm and intercostal and abdominal muscles respectively. The pneumogastrics connect all parts of the respiratory tract with the central nervous system, carrying both afferent and efferent impulses.

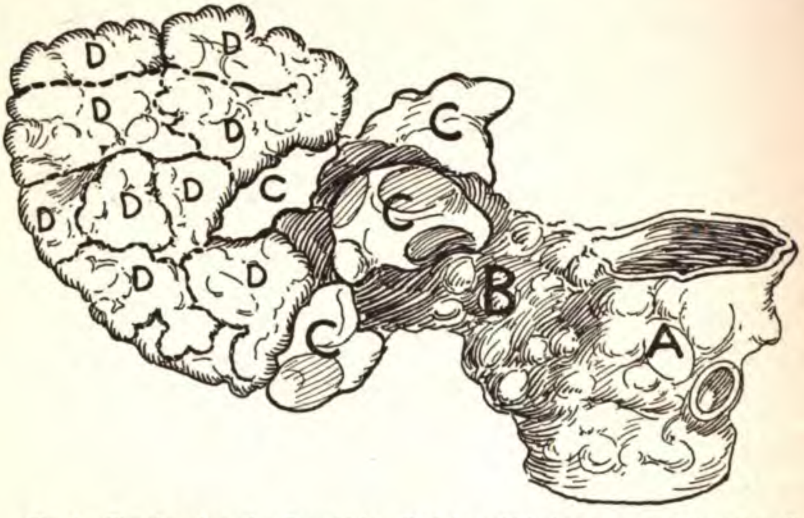

Fig. 3.—The Branches of a Bronchiole. Each bronchiole has numerous divisions; all are irregular. The final endings, the alveoli, are irregular air cells with thin walls. The cross section of the alveoli arising from one bronchiole is far greater than that of the bronchiole. *A,* Respiratory bronchiole; *B,* Alveolar ducts; *C,* Atria; *D,* Air sacs. The finer markings show the alveoli.

But *impulses may reach the respiratory center via almost any* other afferent *nerve, and from the higher centers.* Any irritation of the pulmonary fibers of the vagi, especially of the superior laryngeal branches, may excite cough. Involuntary impulses from the higher centers affect the respiratory center. To prove this it is only necessary to observe the altered breathing of an individual who is the subject of surprise, fright, keen pleasure, etc. The nerves of the skin especially affect the respiratory center. Thermal stimuli, as a cold bath, deepen and accelerate the respiratory movements. Obstetricians slap the buttocks or use thermal stimuli to the skin of a newborn child when it is slow to inaugurate breathing.

The involuntary act of ventilating the lungs depends upon the impulses from the respiratory center sent down the efferent nerves to the muscles of respiraton. These *impulses arise,* it seems, *because of the amount of oxygen and carbon dioxide in the blood circulating through the medulla.* An oversupply of carbon dioxide causes dyspnea. A lack of oxygen causes the same, but less effectively. The two factors together are more potent than either alone. An oversupply of oxygen may cause apnea.

The *center* of respiration is *sensible to* even the *slightest variations in* the amount of *carbonic acid gas but* to only *wide variations in* the amount of *oxygen.* (Stewart.[1]) Campbell, Douglas, Haldane, and Hobson[2] found that a rise of 0.22 per cent in the alveolar carbon dioxide pressure was sufficient to increase the alveolar ventilation of the lungs 100 per cent above the resting phase; they also found that a corresponding diminution in the alveolar carbon dioxide pressure caused apnea.

Whenever the *interchange* of gases between the alveoli and the blood becomes *insufficient, a greater muscular effort is made to ventilate the lungs.* One cannot voluntarily suspend respiration beyond a few minutes. It seems that the respiratory center may be affected through the vagi by the alternate *stretching and relaxing of* the *vesicles* and finer bronchioles. This was demonstrated by Loewy[3] and later Schenck[4] and Ishihara[5] dilated upon and further confirmed the theory.

Christianson and Haldane[6] *found* by means of an apparatus *that when men were compelled to breathe into a bag containing air under a pressure* of 60 to 80 mm. of water, *expiration involuntarily became deeper.* The first effect of the *increased pressure* was a period of apnea, usually of about half a minute. The pause before each succeeding respiration, however, grew less.

A sufficient *stimulation of* the peripheral ends of the *vagi causes* a *narrowing of* the *bronchioles* through a contraction of their muscles. This was proved by Gerlach,[7] by Horvath,[8] by Brodie and Dixon,[9] by Einthoven,[10] and by Beer.[11] The function of the muscles of the bronchi is not known. It has been suggested by Watson-Williams[12] that they dilate the bronchioles to facilitate entrance of air into the alveoli during inspiration, and contract the bronchioles during expiration so as to hold air in longer contact with the pulmonary capillaries.

The *frequency of respiration* in an adult during health is usually around fifteen to twenty per minute. This is variable and readily *affected by* numerous factors, an important one of which is the giving of *attention* by an individual to his own breathing. Increase of body *temperature, exercise, excitement, and many other elements* may increase both the rate and depth of respiration.

A fair *indication of inefficiency in ventilation* of the lungs *is* blueness—cyanosis—of the lips, nails, and skin. This blueness is due to accumulated carbon dioxide.

The blood passes through the *pulmonary circulation* by virtue of the contractions of the right ventricle. The quantity conveyed through the pulmonary vessels with each heart beat must average with that introduced into the systemic circuit at each systole, but the amount discharged with each contraction of the right ventricle need not be exactly the same as that concomitantly discharged by the left.

The *circulation* is *affected by respiration.* As air enters the chest during inspiration and leaves during expiration, so the *flow of blood* into the chest will be *facilitated during inspiration and hindered during expiration.* This has been proved in a number of ways. A blood pressure tracing taken from the carotid artery of an animal simultaneously with a tracing of the respiratory movements shows, if the tracings are in the same vertical plane, that the blood pressure rises with inspiration and falls with expiration. This was first shown by Fredericq.[13] To be exact, the crest of the rise is reached at the end of inspiration and remains for a very brief moment during expiration before falling (Stewart).[1] Erlanger and Festerling,[14] however, found that "in man the sole or main effect of inspiration is to lower the blood pressure." They think the cause probably is the changing capacity of the lung vessels and that this is a much greater factor in large than in small animals, and that in small animals the rise occurs just as has long been thought. Sauerbruch[15] proved in another way that the respiratory phases influence the circulation differently. He made an incision in the lung and observed that bleeding from the incision was greater when the lung was in collapse than when inflated. Cloetta[16] by some ingenious experiments found the same and noticed in addition that the maximum bleeding was just at the beginning of expiration.

The *explanation of the effect which the respiration has on the circulation* is comparatively simple. The *vessels outside the chest have* constantly an external pressure of *one atmosphere.* The *vessels within the chest,* with certain exceptions to be noted later, have an *external pressure greater than atmospheric during expiration and less* than atmospheric *during inspiration.* During inspiration, then, there is a fall, and during expiration a rise in venous blood pressure in both large and small animals. In small animals the arterial tension rises during inspiration and falls during expiration; in man and probably in other large animals the reverse is true. The *increased intravesicular air tension* during expiration, especially if forced, as *in coughing,* sneezing, and dyspnea, *may be* considerable, possibly much greater than *two atmospheres.* Hence the venous blood pressure of the veins outside the chest may greatly exceed the external pressure upon the veins; therefore, the veins just outside the chest will be stretched.

The *heightened* air *tension* within the alveoli will be applied to all structures within the chest and *will affect* the *soft structures.* The *pulmonary capillaries* with the thinnest of walls *receive* the *pressure* direct *and* the *blood is dammed* from them *to* the *pulmonary artery, right heart, vena cava* and thence to the vessels outside the chest. Thus an increased blood pressure of the pulmonary artery and possibly also a *right heart strain,* which may lead to dilatation, is developed.

At this point it is necessary to bring in, in addition to these ordinary facts of physiology, what I have called the "*muffler*" *construction* and action *of* the *lobule* divisions of the lungs. Each bronchiole has three or four or more respiratory bronchioles; and these each in turn, about the same number of atria; these again about the same number of infundibula; and each infundibulum has numerous irregular air cells. The thin partition between any two air cells extends well into the lumen of the infundibulum. From the ramifications of the much branching and rebranching of a bronchiole, there is created in each lobule a maze of blind pockets for air to enter, leave, and reenter before finding the exit. When no force is put on expiration—when expiration is purely passive—air will flow gently and easily by one pocket after the other without entering any, shortly reaching the exit without producing any serious disturbance. But during a forceful expiration air

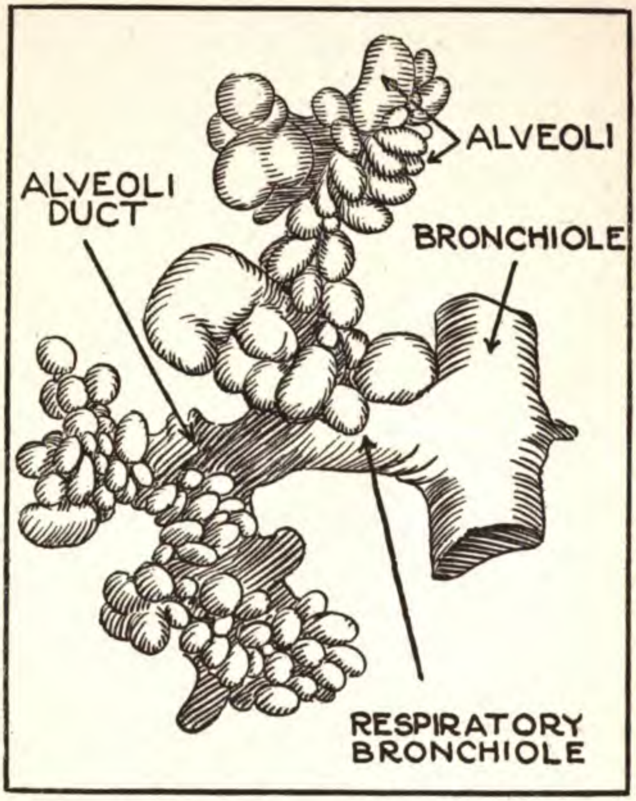

Fig. 4.—The Branches of a Bronchiole, showing irregularities and bulgings which air from a remote air cell traverses to get to the main bronchiole of a lobule. (Gray.)

molecules will rush about from one blind pocket to another, much confusion will prevail, the time consumed in finding the exit will be relatively increased, the intravesicular air tension proportionately heightened and perhaps thereby serious disturbance produced.

One can blow through the muffler of a gasoline motor without difficulty, whereas a cylinder exhausting through the muffler has the momentum of the exhaust air sufficiently reduced to do away almost entirely with the noise of the explosion. The same can be said of a Maxim silencer for a rifle. There are many other *examples.* For instance—a large crowd of people is leaving a building. As long as there is no excitement the egress of the mass is made through the exits of the building with facility and ease. But suppose there is a cry of fire. At once the frightened individuals begin to run here and there from room to room, wherever there is an opening, seeking a way out and not only hinder their own escape but retard that of their companions. This illustration was suggested to me by Dr. Morfit. Even if the lobule had but one wall like a balloon, the application of much pressure from without would cause a proportionate rise of intralobular pressure because the small exit will not allow a sufficiently rapid escape of air to compensate for the increased external pressure.

The increased pressure created within the chest during expiration, especially during a forceful expiration, is developed then in the lobule chiefly before the bronchiole proper is reached. The *tension within* the parts of the *bronchi* which have firm walls then is *not materially altered* during either phase of respiration; therefore the *capillaries of the mucosa* of the bronchi, having the same external pressure as the veins of the neck and other vessels outside the chest, *have the flow of blood and lymph from them accelerated during inspiration and hindered during expiration.*

In the event, then, that the *mucosa* of the comparatively small tubes should be somewhat *swollen and coughing and dyspnea* should *supervene,* the resulting *damming of the blood and lymph to the mucosa during expiration might be sufficient for the exit of air to be seriously impeded.*

A factor which may be active in helping the "muffler" construction of the lobule cut down the momentum of air during forceful expiration is what I have called the *"trap" or "valve" effect.* This is developed in two ways. In the first the division walls of a lobule, projecting into space within the lobule and being soft pliable tissue, may overlap the exit, as the soft rubber valve covering the opening in an atomizer tube directly obstructs the exit of air therefrom. The second manner of obstruction comes about through the increased tension suddenly developed in the infundibula and as suddenly applied to the exterior wall of the bronchioles. This causes the bronchiole wall to be partially collapsed or flattened, interfering with the passage of air through it.

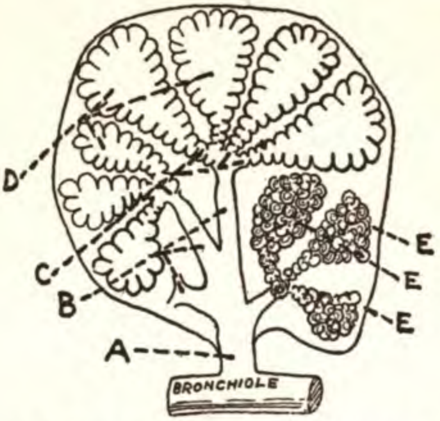

Fig. 5.—Bronchiole. *A*, Respiratory bronchiole; *B*, Alveolar ducts; *C*, Infundibula; and *D* and *E*, Alveoli in a schematic drawing, showing the complicated passages of a lobule.

So far as I know this *"muffler," "valve," and "trap" explanation* has not heretofore been expressed. Lord[17] says of the trap effect, "Expiration, moreover, is accomplished at a greater mechanical disadvantage, for in consequence of insufficient deflation, the alveoli become overdistended and the already constricted bronchioles are still further compressed by an increased intrathoracic pressure."

The two parts of the *heart*, the right and the left, depend for their *nourishment* upon the right and left coronary arteries respectively, both being branches of the aorta. The higher the tension of the blood in the aorta, the greater also will be the amount of nourishment the left heart and likewise the right receives through the coronaries. The lower the aortic pressure, the less is the nourishment of the entire heart, but also the less is the work the left ventricle has to do. It is not necessarily so with the right. The amount of *work the right heart has to perform depends upon the tension of the blood in the pulmonary artery, while the nourishment is in no way regulated by the pressure in that vessel.* This, I believe to be an extremely important fact—and one that so far as I know has not been previously mentioned in literature.

It may be that the right coronary artery constantly carries a surplus of nourishment and thus is always prepared for emergencies. But on the contrary, it seems to me that it will require no stretching of the imagination to picture conditions when the *right heart* may be *doing work out of proportion to* the *nourishment* it receives. Such a condition, it would seem, might result from an extended series of prolonged forceful expirations, as may occur from coughing, or from enlarged lymph nodes or other tumors pressing upon the pulmonary artery or vein.

It has long been known that in certain individuals, many of whom are commonly designated as neurotics, there is a peculiar condition of the finer blood vessels in which they dilate and become greatly overfilled with blood on slight irritation. For example, dragging of a finger or the edge of a percussion hammer handle over the *skin* leaves a reddened *urticarial welt.* It has been noted by Lenhartz and von Strümpell[18] that this obtains especially in asthma.

An *experiment* which will materially help us to understand the physics of an asthmatic attack is as follows. A *rectangular box*—the one I have used is approximately two feet in length by three inches in width and very shallow—without a lid, is *moved rapidly backward and forward* in the direction of the long dimension of the box and in a horizontal plane. While it is going rapidly to and fro, *a marble is dropped into it* near its center. The marble *moves slowly,* first in one direction and then in the other. Each succeeding movement rapidly *adds to its momentum and* also to the *distance it travels* each trip. *After a few moments* it is going from one end of the box to the other with *astonishing speed.* It bumps against one end and in the rebound gets started rapidly back to the other.

*Fluid will behave in the same way* if contained in flexible walls.

The movement of the box is paralleled by placing of tension in extreme portions of the flexible container of the fluid. One can easily picture such conditions with the vessels outside the chest including those within the bronchi as one part and those of the pulmonary vessels as the other part of the container.

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# CHAPTER VII.

## THE PATHOLOGIC PHYSIOLOGY OF SIMPLE DYSPNEA FROM A THEORETICAL STANDPOINT.

From a *theoretical* standpoint the pathology of *dyspnea* must exist in one or more of the following: the nervous system, the muscles of respiration, the mucous membrane of the bronchi, the capillaries, the blood and lymph vessels of the mucosa, the bronchial muscles, deposits or tumors within the alveoli or bronchi, some structure adjacent to the respiratory passages, the heart, the pulmonary circuit, the pleural spaces, or some other organ of the body that may directly or reflexly affect one or more of the above.

For any one of the above factors there may be one or many causes, direct or indirect. For the purpose of this treatise it is only necessary to hint at most of the various theoretical possibilities. The *quality of* the *blood* may be so altered as to bring about labored breathing. Notably there may be too much carbon dioxide, too little oxygen, too much acid or other drug, too much microbic toxine or other foreign albuminous material, fevered blood, etc.

The *carbon dioxide* may accumulate because of overproduction, as by physical exertion, or because of insufficient interchange of gases between the pulmonary capillaries and the alveoli, or because the atmosphere is greatly surcharged with carbonic acid gas. The oxygen may become insufficient because of excessive utilization or from an inadequate interchange of gases in the lungs; or because of a rarefied atmosphere or an atmosphere poor in oxygen.

An *acidemia* may result from the administration of a considerable quantity of acid or because of abnormal metabolic products. These latter occur in diabetes when the body is no longer able to utilize carbohydrates and in individuals from whom carbohydrates are withheld. In either of these instances, fatty acids accumulate by reason of the utilization of adipose tissue for oxidation. Certain drugs which influence the respiratory center or the interchange or metabolism of the gases may be given in too large doses, or for too long a time in nontoxic doses, so that they accumulate in dangerous proportions.

Bacterial or protozoan *toxins* may be absorbed from the alimentary canal, tonsils, abscessed teeth, or other affected areas. Other foreign *protein* may get into the blood from the intestine, respiratory passages, hypodermic injections, or other sources.

The *respiratory center* or its efferent nerves might be so altered chemically that ordinary stimuli would induce excessive action of the respiratory muscles. Or the afferent *nerves* leading to the respiratory center, or centers associated therewith, might be so altered that stimuli usually producing only normal results may affect a normal center so as to increase the activity of the muscles of respiration. The tissues of the body may accumulate heat from the presence of toxic substances or from confinement in too hot a place and from lack of heat dissipation.

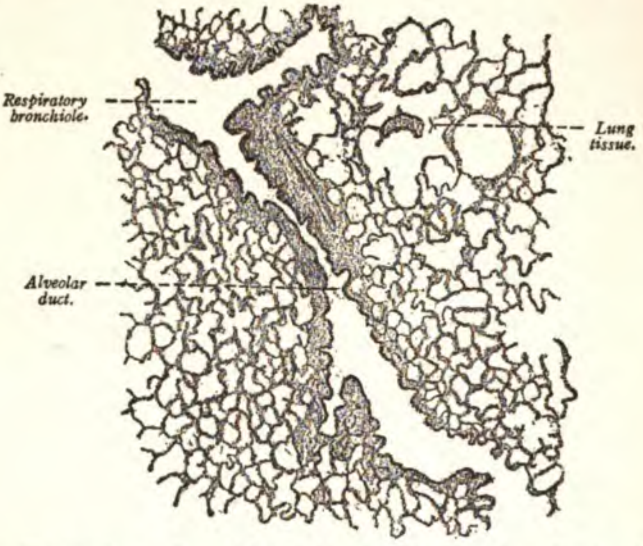

Fig. 6.—The Respiratory Bronchiole and Alveoli in Cross Section. The broad expanse of alveoli comprises a maze of blind pockets in which air may wander around before reaching the respiratory bronchiole. Even after reaching the respiratory bronchiole, the bulgings and indentations of the walls offer additional pockets for air to enter and leave before reaching the bronchiole. (Böhm, Davidoff, and Huber.)

Within the air passages *foreign bodies* or contractures may obstruct the free entrance and exit of air. The foreign bodies may be inspired or they may consist of secretions and hypertrophic processes. They may occur as viscid mucous materials; these may be whipped together by the action of the cilia into casts, pellets, or plugs to block the tubes and hinder the passage of air throughout a considerable portion of the bronchial tree.

The *mucous membrane* of the bronchi may become so *edematous,* or its capillaries and lymph vessels so distended as to greatly narrow the bronchial lumen, thus hindering free passage of air. The *bronchial muscle* might develop a state of *tetany* or spasm sufficient to interfere with the ventilation of the lungs; or the alveoli might be filled with fibrin, serum, or detritus, leaving insufficient space for air.

*Tumors,* as enlarged lymph nodes, thymus, aneurysms, cancer, etc., and fluid in the chest or even in the abdomen may so compromise the trachea, the larger bronchi or the lung space as to afford serious obstruction to the entrance and exit of air. Broken compensation of the heart or an unusual dilatation of the pulmonary capillaries from other causes may hinder a proper interchange of gases between the alveoli and the blood.

Pathologic areas at, or stimuli from, the periphery of the body may excite *reflexes* which may switch to the respiratory center in such a manner as to cause increased action of the muscles of respiration.

Any *two or more of the above* may be *combined,* causing, theoretically at least, a more pronounced dyspnea than would probably be caused by any one factor alone. For example, an aneurysm, pressing on the bronchi, plus a decompensated heart, would bring on a more serious dyspnea than either alone. An acidosis added to this is likely to accentuate the dyspnea, and would certainly complicate and add to the problems of therapy.

# CHAPTER VIII.

## THE PATHOLOGIC PHYSIOLOGY OF ASTHMATIC DYSPNEA—ASTHMA—FROM A THEORETICAL STANDPOINT.

Holding in mind the theoretical causes of simple dyspnea as outlined in the preceding chapter, we are now confronted with the problem of choosing that conception which most rationally explains the *characteristics of asthmatic dyspnea.* The theory selected must answer all of the following questions: (1) Why does this type of dyspnea come in periodic spasmodic attacks? (2) Why is expiration more prolonged than inspiration? (3) Why is expiration actually more difficult than inspiration? (4) Why are there the peculiar sounds from the bronchi? (5) Why is there an excretion with certain more or less typical inclusions? (6) Why does emphysema, temporary if not permanent, always exist? It might facilitate the explanation for us to remember that the cause of one of these symptoms might not be the cause of the others; one might be primary and the others secondary thereto.

An inadequate amount of oxygen or an overaccumulation of carbon dioxide, *acid, drug, protein,* or other substance may inaugurate a dyspnea, and these factors may *occur periodically* and in quantities sufficient to continue a dyspnea for a few minutes or even hours, and hence to this extent simulate asthma.

To illustrate—an individual sensitized to egg albumen may eat egg only at intervals of days and some of it may pass undigested into the blood, there undergoing cleavage and subjecting the individual to whatever physiologic influence the blood split protein exerts on him. Or bacterial *protein* may *accumulate in* an abscess cavity so as to be absorbed at intervals making the effect of the *blood* digested protein *periodic.* This would occur if a pocket of pus were so formed and situated as to fill only at those intervals when the body occupied a certain position. Or as in malarial paroxysms, the toxin may be liberated suddenly and periodically.

An *acidosis* may occur after the ingestion of certain foods. Similar argument may be advanced for *other chemical substances* which may be pictured as having an influence on the act of ventilating the lungs.

These factors, however, can primarily bring about neither an expiration prolonged over inspiration, a *difficult expiration,* sounds in the bronchi, excretions therefrom, nor *emphysema,* and are therefore to be dismissed from consideration except as indirect etiologic factors.

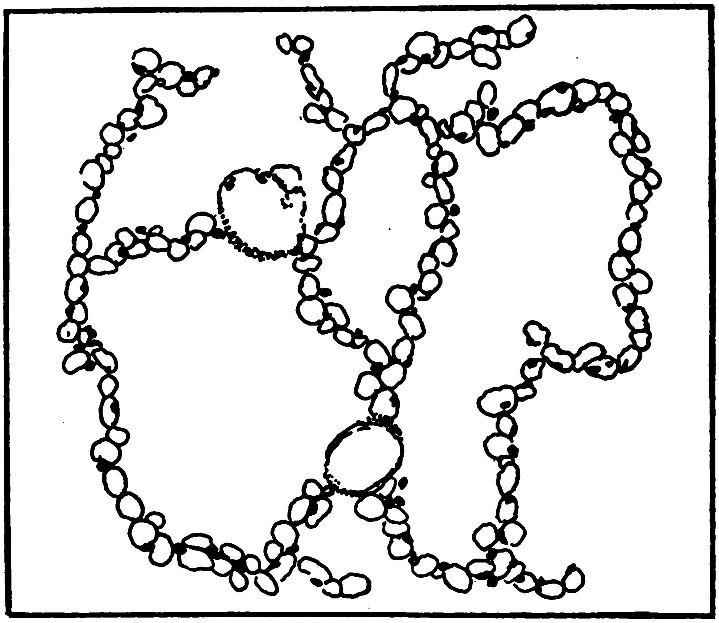

Fig. 7.—The Alveolar Wall and Its Capillaries. The thin walls of the alveoli are thickly studded with the pulmonary capillaries which bulge into the alveolar spaces; a capillary is found on one side of the wall, and the neighboring capillary is on the other side. This alternation is fairly constant. In the partitioning walls, capillaries may be exposed to air and the air tension in two alveoli.

It is difficult to see in what manner organic alterations in the *nervous system,* per se, can be responsible for the periodicity of the attacks of dyspnea, but for the purpose of thoroughness in the introspection of the theoretical possibilities, we will assume that such may be. And when we think of hiccough, accepting the usual explanation of spasm of the diaphragm resulting from a condition in the phrenics or other parts of the nervous system, we might conclude that organic changes in the nervous system may be the essential factor in a convulsive dyspnea. The changes in the nervous system, however, cannot account primarily for any of the characteristics of asthma save the periodicity and perhaps the altered relation of the time of inspiration and expiration; possibly the secretion might be the result of stimuli from the nervous system.

*Foreign bodies* such as pellets of mucus, clots of blood, collections of tissue, etc., generally accumulate periodically and may become so formidable as to obstruct seriously the passage of air into and out of the lungs. Tumors, glands, aneurysms, cysts, etc., pressing from without upon the trachea or larger bronchi may periodically swell so as to offer at these times sufficient obstruction to the breathing to cause it to be labored; or growths within the lumen of the trachea or larger bronchi might do the same. These factors produce labored breathing by obstruction, but both inspiration and expiration are affected similarly, with possibly a slight difference in favor of making inspiration more difficult in case of material in the bronchi, because inspiration tends to carry the material in the tubes toward the narrow diameter whereas expiration does the opposite.

This class of causes also tends to set up *noises in* the *bronchi,* but those of expiration would neither be louder nor more pronounced than those of inspiration. Perhaps even the reverse would be expected, as explained in the preceding paragraph. These causes, too, by irritation might bring about some excretion, but this would be limited. They would not produce emphysema unless the inspiratory forces are greater than the expiratory. The muscles of expiration, chiefly the abdominals, are strong and always well trained and hence are not expected to be easily outdone.

An exception might exist if a *pedunculated tumor* were so situated just beneath the larynx as to obstruct the exit of air by pressing up against the cords during expiration, falling into the trachea during inspiration. This would produce emphysema and a difficult prolonged expiration, permitting easy inspiration, but would not account for the râles, secretions, and circulatory changes. Such a tumor, however, rarely exists.

It can scarcely be conceived that the *bronchial muscles* could in themselves be so altered anatomically or physiologically as to go into periodic contractions without receiving stimuli, but we may assume for the sake of argument that they might be altered so that ordinary stimuli would induce extraordinary contractions. Even if other factors such as foreign proteins, drugs, etc., in the blood, directly through the blood stream or indirectly over the pneumogastrics, should cause these muscles to go into periodic tonic contractions or if the same should result from a pathologic respiratory center, there would be no reason for the expiration becoming prolonged over inspiration. Inspiration and expiration would be made equally difficult unless the muscles would relax during one phase; and this complicates the question by demanding an explanation for the relaxation. Such a condition at best could be only secondary.

In regard to the sounds, it is evident that tonically contracted bronchial muscles must narrow only the finest tubes and hence will produce subcrepitant or slightly coarser râles. Emphysema could not result unless the muscles of inspiration should overpower the abdominals, which seems unlikely. The *bronchial muscle is thin* and *weak* and hence unable to contract with such force as to seriously obstruct the passage of air. More is said of this in a later chapter.

We must hold in mind the possibility that a deposition of *fibrin, serum, mucus,* or other secretions into the alveoli might occur periodically to such an extent as to interfere with the interchange of gases between the air and the blood. This, though, seems to be even more remote than some of the other suggestions, and such factors could not produce any of the other characteristics of asthma.

Periodically *broken cardiac compensation* seems to be a possibility which may frequently be partially responsible for periodic dyspnea; the heart may be able to do its work under ordinary conditions in an entirely compensated manner, and a very small amount of extra work may suffice to bring on the break in compensation—this, in turn, readily disappearing after a brief period of rest. But this cannot primarily produce any of the other characteristics of asthma.

*Stimuli from* the *periphery* or other points far distant from the lungs may be reflected to the lungs, but can only secondarily affect the breathing so as to cause any of the characteristics of asthma save that alone of periodicity.

Forms of edema known as angioneurotic occur at times and may be the essential cause of a periodic dyspnea; and either passive or active *congestion* of the ordinary type, of blood and lymph in the vessels of the bronchial mucosa may come periodically and may well be of such degree as to cause labored breathing. Inflammation is included in this. These, if of sufficient grade, would produce difficult inspiration, difficult expiration, noises perhaps characteristic of asthma, excretions likely with the usual inclusions of asthmatic sputum; but there is no reason why these factors should produce either relatively prolonged and difficult expiration as compared with inspiration or emphysema unless some element is concerned which would cause a variation of the amount of fluid in the bronchi during the two phases of respiration.

An *increased tension of the intravesicular air* occurs, of course, only during expiration. It dams the blood and lymph from the chest where the air pressure is more than atmospheric to areas where the pressure is but one atmosphere. The bronchial mucosa as explained in a preceding chapter is submitted constantly to practically one atmospheric pressure. During inspiration the fluid will be withdrawn—inspired—from these areas of atmospheric tension into the chest where the tension is less than one atmosphere. In the event that a sufficiently increased intravesicular air tension arises, damming of the fluids to the bronchial mucosa will occur to such an extent as to seriously occlude the tubes—during expiration only, never during inspiration—bringing about labored, prolonged, difficult expiration, mucous secretions with detritus, râles especially during expiration, and, since air gets into the chest easily and out of it with difficulty, emphysema. If the cause of the periods of heightened tension of the alveolar spaces comes on periodically, then all the characteristics of asthmatic dyspnea may be produced by increased intravesicular air tension.

Since increased intravesicular air tension occurs with any *nonpassive expiration,* and since nonpassive expiration is a part of all dyspnea, coughing, sneezing, etc., it can be seen that all causes of simple dyspnea may theoretically be connected indirectly with the production of asthma, but that irrespective of inflammation, the causes of dyspnea, the action of bronchiolar muscle, the effect of nerves or the nervous system, the one essential element leading to all the signs characteristic of asthma is NONPASSIVE EXPIRATION. This will be taken up in detail in the next chapter.

# CHAPTER IX.

## THE NONPASSIVE EXPIRATION THEORY OF ASTHMA.

I hold that asthmatic dyspnea is essentially a *mechanical interference* with the *bronchial* blood and lymph *circulation,* due to heightened intraalveolar tension, and that this arises from nonpassive expiration. The more active and prolonged the expirations, all other contributing forces being equal, the more likely will there result a degree of congestion sufficient to impede the exit of air. Coughing, sneezing, and a morbid attention to the act of respiration, etc., make expiration an active muscular effort instead of a passive one.

I especially emphasize the prominent part played in many instances by coughing and sneezing. As *coughing* consists of sudden forceful expirations, and as it is escaped by no individual, it is consequently the most potent factor. When cough supersedes cough in rapid fierce succession, and the terrible paroxysms last for many minutes or even hours, recurring, as in many cases, two, three, four times, and even more, daily for months or years, the increased intraalveolar tension caused thereby becomes a factor of *great potency in affecting the thin structure of the lungs and bronchi.*

An accumulation of lymph and blood may be caused in any part of the body by *inflammation.* So in the bronchi, inflammation greatly *facilitates,* and in most cases probably is absolutely essential for the development of that *grade of swelling* which exists *in asthma.* The *inflammatory processes* in the bronchi are also a *cause* of that essential element—the *nonpassive expiration.*

It is theoretically possible for *nonpassive expiration,* unassisted by inflammation of the bronchi, to cause asthma. Experiments which indicate the possibility of this are on record, but that this occurs except by pure experiment, I am inclined to doubt. Reference is made to this in a later chapter.

An *angioneurotic edema* or an urticarial condition of the bronchi may have much the same effect as will a more chronic inflammation. In this way an anaphylactic reaction may suddenly initiate an attack of asthmatic dyspnea.

Any condition or factor which causes an ordinary dyspnea, or which results in an application of force to expiration, may bring on asthmatic dyspnea. Whether the *asthmatic dyspnea* develops or not will *depend* (1) *upon* the amount of force put upon *expiration;* (2) upon the *strength of the walls of the capillaries* and lymph channels of the bronchial mucosa; *and* (3) upon the grade and type of the *inflammatory processes* within the bronchi.

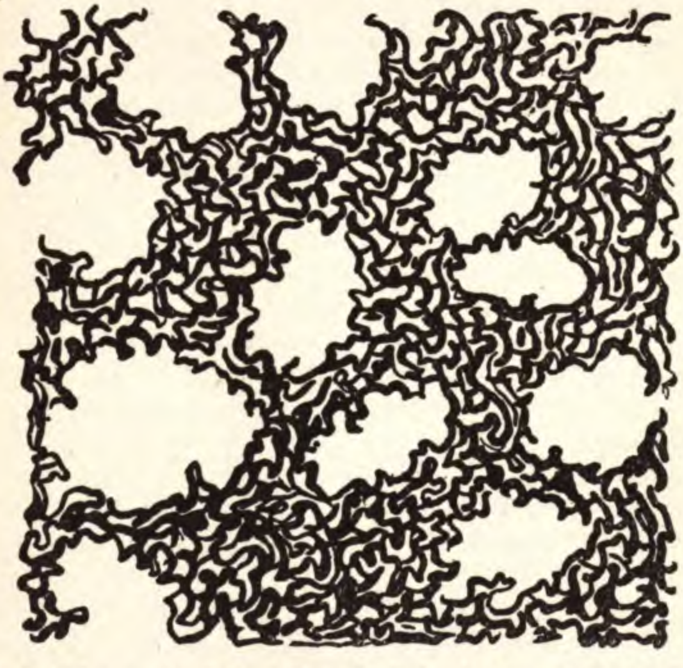

Fig. 8.—Pulmonary Capillaries. The walls of the alveoli are thickly studded with capillaries; any marked alteration of alveolar air tension will therefore have a profound effect upon the circulation. (Böhm, Davidoff, and Huber.)

*Many factors* may be concerned, and to such an extent that they become essentially primary. In one case a certain element may be of great importance, while in another a wholly dissimilar one is of prime significance. This helps to account for the varied conceptions of this affection.

For the sake of those who have not read the preceding chapters carefully, it may be well to explain *in what manner nonpassive expiration interferes* with the circulation of blood and lymph through the bronchial mucosa. At the instant that muscular force is applied to the act of expiration, the air in the many cells, infundibula and ducts leading to a bronchiole is placed under greater pressure than occurs in a passive expiration. Because the bronchiole is very small as compared with the expanse of its branches, it is impossible for the air to escape as suddenly as the force is applied. Hence the pressure may be steadily increased or but slightly lessened during the entire expiratory act. A bronchiole is completely surrounded by air vesicles, and the vesicular pressure, concomitantly with the act of expiration, is applied to all the structures within the chest, including the external walls of the bronchiole, thus tending to cause the thin-walled bronchiole to collapse.

The bronchioles are branches of the *larger bronchi* which *have cartilage* and fibrous tissue in their walls and hence the air tension upon the inside of the bronchi, unless occluded higher up by edema, dilated vessels, glandular products, or other processes, is practically that of the external atmosphere. Therefore, it is only the *endings* of the fine bronchioles which *may* possibly *collapse* with forceful expiration. Hence, *the more one tries* to force air out, *the greater will be the compression* of the bronchiole; and the more the obstruction increases, the greater must be the effort to expire. Collapse of the bronchioles is probably not an important cause of dyspnea; and after asthma has existed for a time, the bronchioles may actually dilate because of the obstruction higher up, as is explained later.

What appears to me to be of greater significance and even more plausible is that the construction of a lobule with the branches and divisions of the infundibular ducts, infundibula, and cells of soft pliable tissue is that of a "*muffler*" or "silencer" plus that of a "*valve*" or "*trap.*" A Maxim silencer on a rifle or a muffler on a gasoline engine, because of blind pockets which air will enter and leave before finding the exit, reduces the momentum of the air to such an extent that the noise of the explosions is remarkably decreased. Or, as suggested by Dr. J. C. Morfit, if a large number of people in a hall attempt under the force of fright to pass out through a single exit, consternation and confusion will prevail and the departure of the crowd will be greatly hindered. While one may blow through a "muffler" without appreciable hindrance, a cylinder of an engine exhausts through it with a tremendous interference and the reduction of the momentum of the air passing through the "muffler" will be proportionate to the air's momentum. In addition to this is a valve effect which, it must be admitted, is problematical, but theoretically it is active. Thin rubber on the end of a tube projecting into a rubber bulb may seriously interfere with or entirely block the egress of air when the bulb is forcibly squeezed; slow gentle pressure of the bulb may empty it completely with no interference from the valve-like rubber flap. In these ways the air tension within the alveoli becomes increased during forceful expiration, affecting all the soft structures within the chest, whereas the air tension within the bronchi, until occluded by swelling, is approximately that of one atmosphere.

When the intraalveolar air tension is definitely increased, two other factors than those given above become active toward keeping the increased tension established. I refer to *the stretching of the alveoli* and to the *expiring against pressure*. These two factors may in reality be only one. It has been shown that when the walls of the alveoli are stretched—when the cells are in the position of full inspiration—there is a tendency for expiration to be reflexly initiated. Since there is constantly an emphysemic condition of the alveoli during attacks, there is a tendency for the respiratory center to be constantly receiving efferent impulses from the alveoli demanding expiration.

In the attacks the asthmatic is consistently exhaling against a pressure much above normal, and since exhaling against pressure calls forth a more forceful expiratory effort, the tendency is for the pressure to gradually and constantly grow, creating another vicious circle.

The pressure applied to the *bronchial* vein dams the blood to the *capillaries* of the firm-walled bronchi; the capillaries within the bronchi are subject to a practically constant pressure of one atmosphere while the pressure upon the bronchial vein during expiration is always greater than one atmosphere, and may be very much greater. The bronchial lymph channels and their branches are affected similarly to the bronchial vein and its capillaries.

The pulmonary capillaries, as has been said, receive on their external walls the force of the intraalveolar tension, and hence the blood is dammed to the pulmonary artery and left ventricle and through it to the right auricle and the great veins to the bronchial vein. This will further the *damming of the blood into the lumen of the bronchi.* Then again the pulmonary capillaries anastomose with the capillaries of the bronchi, and as the tension of the air against the former increases, the blood passes from them to the bronchial capillaries. Another factor perhaps of considerable importance in causing an overfilling of the blood vessels of the mucosa is the arterial tension, which, according to recent experimental evidence, is heightened during expiration. Theoretically at least, the rise in the blood pressure is proportional to the force and rapidity of exhalation, and will to the same degree be increasingly

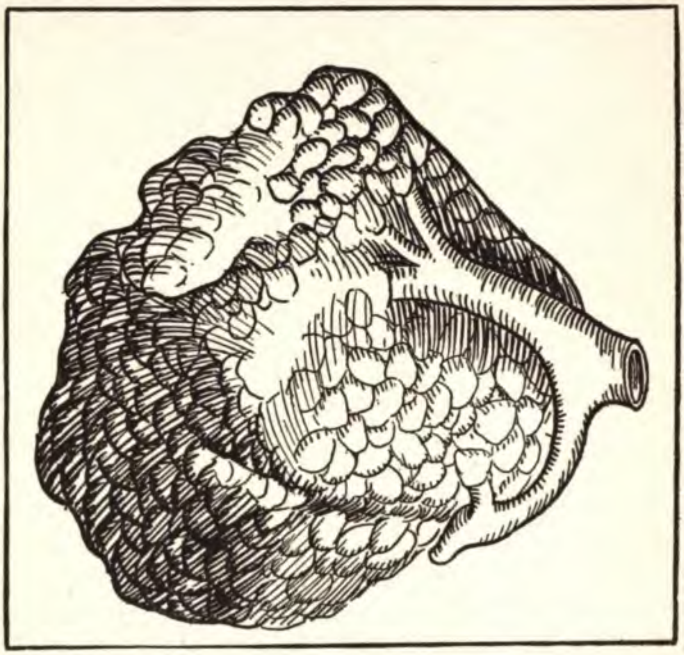

Fig. 9.—The Lobule. The respiratory bronchioles, alveolar ducts, atria, infundibula, and alveoli constitute a many-celled balloon with the bronchiole as the exit. If no other force than the natural elasticity of the tissue is used to expel the air from the many cells of a lobule, the air will flow uninterruptedly through the bronchiole and the pressure within the lobule will be raised but little above atmospheric pressure. But if more force is used in expiration, the air will leave the lobule more rapidly but a greatly heightened tension within the lobule will be engendered. (Gray.)

active in forcing blood into the overfilled capillaries of the mucosa. The greater the swelling of the bronchial mucosa, the more force is needed to effect expiration; and the more force used, the greater the swelling. This is a vicious circle.

The *right heart* must, on account of the damming of the blood into the pulmonary artery, work a great deal of the time against a much *greater blood pressure than is customary.* It does this, too, without a proportionate increase in its nourishment, since the blood supply to the right ventricle and auricle is proportionate to the blood pressure in the aorta. This factor weakens and dilates the right heart, and will further dam the blood into the large veins, bronchial veins, and capillaries. Therefore, a previously weakened right heart becomes an important contributing cause of asthma.

*Bronchitis,* which is an important element in the production of asthma, *may hinge upon* one or more of several factors. The most common one I believe to be latent or slightly active pulmonary foci of *tuberculosis.* Bronchitis from such a cause will be made more active by infections in other parts of the body, as for instance, a pyorrhea, an alveolar abscess, a tonsillitis, a sinusitis, an appendicitis, an endometritis, a prostatitis, etc. These foci may feed bacteria into the blood or lymph streams to locate in the already mildly inflamed bronchi; or the bacteria may travel there by direct extension. Bronchitis may be solely caused by bacteria through direct extension or through the blood stream from an infection in the upper respiratory tract. If this latter process is chronic, the resultant bronchitis may be chronic even in the absence of pulmonary tuberculosis.

In hay fever or other *anaphylaxis* involving the respiratory passages, the vasomotor distention and accompanying infection may travel down the trachea to the bronchi, and if of sufficient intensity, duration and frequency, the abnormal breathing, coughing, and sneezing may bring about an asthmatic condition.

The *horizontal position* tends to precipitate an asthmatic attack because of overfilling of the larger veins. *Worry, excitement,* physical exertion, etc., will cause labored breathing and hence forceful expiration and possibly an attack of asthma; or worry and exertion may set up coughing and sneezing and thus bring on a paroxysm. Reflexes from any source may cause labored breathing and nonpassive expiration.

*Coughing* tends especially to cause swelling of the capillaries and lymph channels of the bronchial mucosa, and is the chief factor in causing asthmatic dyspnea. But it also *expels mucus* and other detritus from the respiratory passages, and therefore may actually, though doing temporary injury, remove the material causing the irritation and nonpassive expiration, and bring about cessation of an attack.

In the event that *bronchial muscle spasm* results from anaphylaxis or from nasal or other reflex, it would help to induce the circulatory changes here detailed by first producing a simple dyspnea.

*Emphysema,* it will be seen, necessarily develops hand in hand with asthma, and arises from the same causes. As congestion and inflammation of the bronchi cause increased activity of the glands of the mucosa, the accumulation of mucus may soon become a serious additional obstruction to breathing. Then, too, as the mucus accumulates and the congestion increases, there is greater opportunity for the growth of bacteria—and thus develops still another vicious circle.

*An attack,* as is well known, *may cease* without treatment. This is because the patient may learn to breathe with a comparatively passive expiration or because the otherwise relatively little used expiratory muscles become fatigued and unable to continue the forceful expirations; or through the expectoration of particles which have been the chief source of the irritation in the trachea or larynx, the coughing and other forceful expiration ceases; or the patient may actually get rid of mucus which seriously obstructs breathing; or simply having the impression that the mucus is choking him, he dislodges it, his fright ceases, respiration becomes a nonsubjective, naturally involuntary and passive process.

Summarizing the effects of the increased vesicular air tension, we find that it acts, (1) by pressing directly upon the bronchial vein and interfering with flow of blood from the bronchial capillaries; (2) by pressing upon the bronchial lymph duct and damming lymph to the bronchial mucosa; (3) by pressing upon the pulmonary capillaries, damming blood to the pulmonary artery and the right heart, possibly straining the right heart, but at any rate raising the venous blood pressure and hindering the emptying of the bronchial capillaries; (4) by pressing upon the pulmonary capillaries and causing a flow of blood through the anastomosing capillaries to the bronchial capillaries; (5) by pressing upon the pulmonary capillaries and forcing blood to the pulmonary vein and left heart, and consequently raising the arterial blood tension and incidentally bringing about greater congestion in the bronchial mucosa; (6) the more the circulation within the mucosa is interfered with, the more likely will there be an increase in the activity in the bronchitis; (7) the greater the mucosa congestion and inflammation, the greater the edema; (8) as the severity of the congestion and inflammation increases, the greater will be the amount of mucus, pus and other inflammatory products; (9) the more the inflammatory and other detritus within the bronchi, the more it interferes with the passage of air, and the more it irritates the hypersensitive nerve endings of the mucosa; (10) the emphysema which develops sets up in the nerve endings of the afferent vagus fibers stimuli which, reaching the respiratory center, tend to reflexly impel expiration; (11) the intravesicular pressure which arises tends to cause more forceful and complete expiration; (12) the more severe all these factors, the greater will be the effort to expire—thus being established the serious vicious circle responsible for asthma.

# CHAPTER X.

## THE DEVELOPMENT OF THE NONPASSIVE EXPIRATION THEORY.

During the fall of 1907 there was sent to the Missouri State Sanatorium of which I was then in charge, a *tuberculous patient* who also suffered paroxysmal attacks of expiratory dyspnea of a very high grade.

The institution was small at that time, there being but four or five patients. I occupied a room in the building with the patients. The *asthma attacks* in this case came fairly regularly, usually at the rate of four or five per twenty-four hours. All that I did or had done for them seemed to be of no avail and each attack endured one to two hours, causing not only the patient but the physician in charge much suffering.

Up to this time I had had but little *experience* in the treatment of a small number of cases of asthma. For the most part, these had been given relief by such drugs as lobelia, morphin, potassium iodide, etc. But it was not so in the case of this man whose breathing and distress awakened me at least once or twice a night for about three weeks.

It is neither necessary nor possible for me to enumerate the *remedies* which I used in this case. Suffice it to say that they were those that are ordinarily recommended in the textbooks as being of value in asthma. Whether any of them were really of value or not, except as hereinafter detailed, cannot be stated because I do not know how long his attacks would have lasted had he been given nothing; but I do know that the drugs seemed to have no more effect than so much water. I had always been taught that the "sheet anchor" of all remedies for the acute attacks is morphin. But in ¼ grain doses it did him very little if any good. Why I did not use larger doses I cannot say, but this was early in my medical career.

The patient had a *mitral murmur* which apparently was perfectly compensated, but in my desperation, after days of noneffective treatment, I reasoned that perhaps the dyspnea might be a cardiac affair and therefore I tried the various remedial agents which are ordinarily recommended for cardiac dyspnea. These also did him no good. No matter what else was administered, I gave an injection of morphin before the attack ended.

For one of these attacks the patient was given *strychnin*—1/20 grain hypodermatically—*and* the results were none or very slight. When I was satisfied that no benefit was coming from it, ¼ grain of *morphin* was injected. Almost as rapidly as I am setting down these words, relief began to be evident, and in about five minutes was complete. I at once felt that my previous observation as to the value of the morphin had been erroneous. The next attack soon developed and I administered a dose of morphin. When fifteen or twenty minutes had passed with little or no change in the condition of the patient, 1/20 grain of strychnin was given and just as speedily as before relief was afforded.

This simple experiment was repeated time after time, always with the same satisfactory results. At this time I argued that the *morphin* allayed the irritation which caused the coughing *and* quieted the spasm—perhaps of bronchial, perhaps of psychical origin—and that the *strychnin* did something to the circulation. Just what change was induced in the circulation I did not know, but it seemed to me that change there must be; and I argued further that if the whole or essential cause was a spasm of the bronchial muscle fibers, strychnin, if having any *effect,* would tend to increase the tonicity of these fibers and to do harm rather than good.

I had also observed that *every attack* of the asthmatic dyspnea was *preceded by severe coughing.* To this day I have a vivid mental picture of those attacks. The night paroxysms seemed to be the most distressing. In the inception of an attack the coughing was easy, becoming gradually worse. As it became more frequent, severe, and prolonged, the breathing gradually grew more labored. Usually the coughing became paroxysmal so that the time for inspiration was greatly reduced. If the patient stopped coughing for a few free breaths, it was observed that both inspiration and expiration were becoming labored and after a little while there was another decided change in breathing, inspiration growing relatively easy and expiration more difficult. This I repeatedly observed.

I also noticed in this patient what I dare say everyone has seen; namely, during severe coughing fits the face became very red and the veins of the neck dilated greatly. This *showed me conclusively* that during the attacks, in this case at least, *there was some change in the circulation.*

It occurred to me that if the combination of strychnin and morphin would so efficaciously relieve, surely they would, when given at the proper time, *prevent* the *attacks.* After putting this thought into action, the man had no more paroxysms as long as he was under my care. He took by mouth the amount of the drugs he had been taking by the needle and before the attacks showed signs of developing, which made the doses about four to six hours apart. I even took him to his home two hundred miles away without a paroxysm developing. A few days afterward, however, the man died in one of the attacks.

At the Sanatorium I had three other cases of asthma. One of these taught me, in addition to what I had learned from the case just described, these two important points; firstly, her only attack of asthma followed *immoderate exercise,* and secondly, relief from the paroxysm came rather promptly when I experimentally instructed her to *breathe* naturally in slow *deliberate* fashion. The other two cases taught me relatively little except for the increased conviction that circulatory disturbances must be a factor in asthma.

These four patients gave me opportunity to *study* a *large number of attacks*—perhaps fifty or more—from beginning to end, watching the paroxysm develop, pass through the climax, and decline, in many instances without being appreciably influenced by drugs or other therapy. It was fortunate for this work that the paroxysms of my first case were uninfluenced by morphin. Otherwise I probably would not have given such an amount of thought and study to his attacks.

Four years' experience as visiting physician to the St. Louis City Hospital gave me further opportunity to study asthma. During this time we took one of my patients into our home as a maid in order that I might again have the opportunity of seeing the beginning, climax, and ending of attacks. This afforded me unusual advantages, as I was thus enabled to see her in numerous attacks. My experience in private and consultation practice has given me opportunity to see many patients with asthma, but *the few cases* I studied at practically all hours of the day and night were by far the *most helpful.* It was seldom in either hospital or private practice that I was privileged to see patients in acute attacks. In two patients, one in my home and the other in the Sanatorium, I saw over 50 paroxysms, and in 45 patients I did not see over five paroxysms. It is rare that a physician is privileged to see an attack develop, culminate in a climax, and subside.

After finding that attacks of asthma could be prevented by giving regularly doses of strychnin and morphin in combination, it occurred to me that perhaps the *strychnin alone* might suffice to prevent the attacks. This did not always prevent, but it seemed to have a positive tendency to do so.

About this stage in the development of my ideas I began to believe that *right heart strain* was the paramount factor in asthma. So consequently I gave digitalis and I was convinced that beneficial results were obtained. Combined with strychnin, it seems to be still surer in its action.

The idea of *right heart* playing the important part held the *center of* the *arena* for my thoughts for a period of nearly four years. During this time I began to explain to myself and to my classes the weaknesses of the existing theories.

About two years ago there came to me the idea that the *endobronchial pressure differs* from the *intraalveolar during* coughing—because of the "muffler" and "trap" construction of the lobules. Later I realized that simple dyspnea, sneezing, laughing, etc., were forms of nonpassive expiration and had the same influence as coughing, varying only in degree.

# CHAPTER XI.

## PROOF OF THE NONPASSIVE EXPIRATION THEORY.

My theory of asthmatic dyspnea developed from, and found *first substantiation* in my own clinical studies. A protracted study of the physiology of the circulation of the lungs, bronchi, and heart was made, however, before light began to dawn upon the details. The essential facts of the anatomy and physiology have been set forth in preceding chapters and I present my clinical studies in detail in a later chapter.

*Best proof* that asthma results from nonpassive expiration can be obtained by any physician with *an asthmatic patient* and a stethoscope. First, if the patient is relatively free from asthma, instruct him to breathe with a slow easy inspiration and a slow easy expiration. The breath sounds will usually be found to become clearer before he has taken many breaths,—the sounds will at least not be intensified. Second, have him breathe with slow easy inspiration but with quick *forceful complete expiration.* If he has an asthmatic tendency at this time it will take but a very few such breaths to *cause many loud whistling piping râles to appear* on expiration. The first forceful prolonged expiration will increase the intensity of the sounds and if the patient is much asthmatic it will take only three or four of them to make the râles prominent. It will be found usually that the dyspnea becomes distressing after but three or four minutes or even less of such breathing.

Third, instruct the patient to make *inhalation quick and complete* and likewise exhalation quick, muscular, and complete. This will not materially change the character of the sounds. Fourth, order the patient to continue the same type of inspiration; i. e., quick and complete but to make *expiration* easy, deliberate and *slow.* The intensity of the *noises* will promptly *decrease* and after a few minutes of such breathing there will be a marked disappearance of the whistling piping râles. The longer he breathes in this manner, the clearer, as a rule, will the sounds become. The mucus and other detritus present in the tubes cannot be removed by this procedure and hence they continue to make noises and may prevent the breath sounds from becoming entirely clear.

I know a physician who demonstrated *asthmatic* breathing to his wife by *imitation.* He practiced forceful prolonged expiration for some minutes without thought of the consequences. He *developed an asthmatic wheezing respiration* which lasted for 30 minutes. He concluded he would never again demonstrate asthmatic breathing to anyone. This man's bronchial mucosa surely could not have been entirely normal or he would not have developed the asthmatic dyspnea so readily. I believe that any man can, however, by a sufficient amount of practicing forceful prolonged expirations cause his breathing to become asthmatic.

I have studied more than 50 cases of asthma since the study of the *one case* which *excited this work.* But from all these 50 cases I have not learned as much as from that one case. The amount of time spent on it I am quite sure far exceeds that spent on all the others.

Without reviewing in detail the history of this case, suffice it to say that my study of it made some *indelible impressions* upon my mind; namely, (1) bronchitis and coughing preceded the first attack of asthma by months, perhaps by years; (2) every attack of asthma was preceded by severe incessant paroxysms of coughing; (3) the cause of bronchitis was tuberculosis—at least the bacilli were found in the sputum; (4) there were marked circulatory disturbances during the coughing spells as evidenced by the puffiness and redness of the face and the distention of the neck veins; (5) I then reasoned that there must consequently be a right heart strain during the coughing spells; (6) the fact that the combination of morphin and strychnin relieved the attack whereas neither drug by itself had any perceptible influence convinced me that a sedative for the cough and a stimulant for the circulation was of benefit in relieving the attacks; (7) the use of morphin and strychnin at proper intervals prevented the attacks.

Study of subsequent cases has shown me the *reliability of* my early *observations.* Every case of asthma I have seen has given a history of respiratory tract inflammation of weeks, more often of months or even years duration preceding the appearance of the asthma. It has not been possible to trace accurately the cause of the infection in most cases.

My investigation began with *no preconceived notions.* From what I had been taught concerning asthma, I had not been able to get an explanation which was at all satisfying. There was no tendency to crystallization of my ideas until six years after my studies began. Therefore my records are incomplete, especially as regards foci of infection and other details. Alveolar abscesses, pyorrhea, and other mild infections did not keenly attract attention formerly. I have not been able to exclude tuberculosis in any of my cases. I have found tubercle bacilli in something over 10 per cent of them and in around 90 per cent there were positive signs

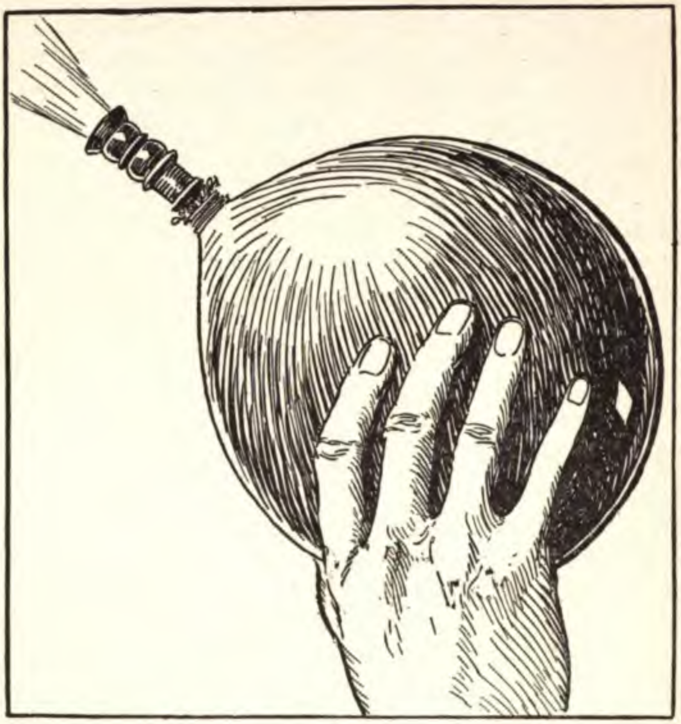

Fig. 10.—A Toy Balloon. A small rubber balloon when inflated with air has an internal tension by virtue of the amount of air in the balloon and the strength of the rubber in the wall. This internal tension of the balloon at the end of inflation may be compared to the intralobular air tension at the beginning of expiration. A squeezing of the balloon by the hands will cause the internal pressure to be increased. When force is applied to expiration, the tension within the lobule is similarly heightened.

of lung tuberculosis. In a small percentage the only cause of the bronchitis seemed to lie in the nose or contiguous parts of the respiratory tract, or had its origin in hay fever.

Even in those cases of asthma associated with *hay fever,* the *asthma* did not come on with the beginning of the hay fever but only after it had made its appearance for a number of years, usually no less than from six to ten.

The *dyspnea* did not begin suddenly in any case, even in those that had had the attacks for years. I wish to emphasize that it always *began gradually* and as the paroxysms of coughing continued, or as the patient became more nervous and frightened, the intensity of the asthma increased. There seems to be an opinion among the medical profession that asthma may develop suddenly, striking an individual in good health like a bolt of lightning from a clear sky. Nothing in my experience warrants this assumption.

The *dyspnea* at first is always *inspiratory as well as expiratory* and as the breathing gets quicker and more muscular effort is expended on both phases, the inspiration gradually becomes easier and shorter while expiration lengthens and becomes more labored and difficult.

*Pathologic changes* sufficient to keep up an infection in the respiratory tract with coughing, sneezing, or labored breathing *always exist.* These foci of infection may be in the nose, sinuses, mouth, gums, tonsils, lymph glands or elsewhere about the body. Latent, but *slightly active tuberculous foci* in the lungs, even in people without signs of bronchitis, are extremely *common,* so common that no one dares to estimate them; and some internists are not sure but that they find signs of trouble, perhaps healed, in nearly every chest examined. No focus of infection can more readily keep up bronchitis than a tuberculous one in the pulmonary tissue, especially if complicated with pyorrhea, alveolar abscesses, infected tonsils, catarrh of the nose, a sinusitis, or other foci of infection about the respiratory tract. Then, too, these common lesions of the nose, pharynx, and contiguous structures may easily spread to the bronchi and become the primary cause of a chronic bronchitis, perhaps in the absence of tuberculosis.

Hay fever, egg *anaphylaxis,* etc., may be considered as included in the above. Then, too, a *mixed infection* anywhere in the body may supply organisms to a tuberculous focus in the lungs and make a mixed infection of what otherwise might be a simple tubercle bacilli growth. It seems reasonable that this may occur from an appendicitis as well as from a tonsillitis, from a salpingitis as well as from a pyorrhea, from a cholecystitis as well as from a sinusitis, etc. I have come to the conclusion from the study of my own cases, that tuberculosis is surely an important primary etiologic factor in a considerable percentage of asthmas, and may actually need to be considered in nearly all.

*To offset my prejudices,* my seeing those things and only those that I have learned to look for, *I* prefer to *present* in the main the recorded *observations of others* to support my contentions. Then, too, the experiences of even a comparatively small number of those who have studied and written on asthma is so much greater than any one clinician could ever have. As no one has had just my conceptions of asthma, and most men have had ideas radically different from mine, their observations should be of peculiar significance, if supportive of my theories. I believe that my theories can be proved, (1) by a study of the patients who suffer from asthma or (2) by a study of the cases recorded in the literature or (3) by a study of the facts of the physiology of the heart, lungs, and bronchi. A report of a number of my cases together with case records from the literature are given in a subsequent chapter. The physiology of the heart, lungs, and bronchi, and the application thereof in the explanation of asthma is given in preceding chapters.

It is not only unique but significant and convincing that I can turn to that splendid book by *Henry Hyde Salter*[1] and find proof of my theories in his observations. He says, "If we could see into an asthmatic during a fit, we should see a certain dose of the same deranged distribution of blood and from the same cause—arrest of the pulmonary circulation from the shutting off of air. We should see pulmonary arterial congestion, *distended right heart, large veins full,* and a scanty supply of imperfectly arterialized blood finding its way to the left ventricle. All external manifestations are consistent with this; the small and feeble pulse, the irregular and faltering systole, the turgid veins of the head and neck, the occasional hemoptysis, the dusky skin."

Salter refers to *talking, laughing, coughing, sneezing, prolonged expiration, overexertion, nervousness, cold, heat, weather changes, etc.,* as *factors in* the development of *asthma.* Of laughing he says, "I have known several cases of hay fever in which, although the individuals could laugh with impunity at other times, yet during the hay season they never dared laugh lest it should make them asthmatic. I believe it possesses this tendency by producing a condition of extreme expiration. There is no doubt that this favors asthma. I have known many patients who could always make themselves decidedly asthmatic (when the thing was hanging about them) by making two or three prolonged expirations, and emptying the chest of air; the same kind of a thing that a person does when you tell him to wheeze."

Not the least *important proof* of my theories, I hold *is* the well known fact of physiology, that the arterial *blood pressure in small animals rises during* the greater part of *inspiration and falls during* the greater part of *expiration.* Of equal importance is the observation of Sauerbruch[2] that an incision in the lung bleeds more when the lung is in collapse than when inflated. Cloetta[3] showed that bleeding of the lung incision was greater during inspiration and the very beginning of expiration than during the remainder of expiration.

Perhaps the most complete substantiation of my conception of asthmatic dyspnea is found in the *experimental work of von Strübing.*[4] He instructed some of his *students to imitate the respiratory movements of asthmatics.* This means they were to expire forcibly. The students *found* after they practiced this type of breathing for a time *that they developed decided signs of asthma.* They discovered also that even mildly inflammatory conditions of the respiratory passages helped in the development of the symptoms; especially efficacious in causing the evidences of asthma to appear was the cough which came with "colds."

*One* of the students, after he had become adept at creating signs of asthma, *acquired* a severe *bronchitis,* during the course of which he unexpectedly developed one night a violent *and most distressing attack of asthma.* He found that *when he could control his expiration,* executing the act without muscular effort, *he could breathe* more *comfortably.* But the desire to cough was so utterly uncontrollable at times that all efforts to breathe properly were of no avail. This student's health was impaired for a year in spite of his efforts to breathe normally and to recover from the bronchitis. The essential conclusions at which von Strübing arrived were that if breathing with a nonpassive expiration is sufficient to cause the development of signs of asthma, the way to relieve the attacks is to regulate the breathing so that expiration is absolutely passive.

*This set of experiments, if confirmed, would prove my contention.* But the character of the experiments is such that the results are apt to be serious. No individual has a desire to develop a condition which renders him susceptible to asthma. Any asthmatic with evidence of an attack can by a few forceful expirations markedly in-

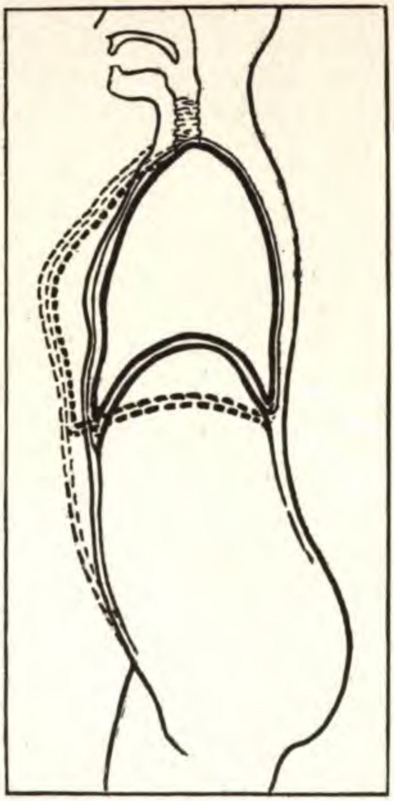

Fig. 11.—The Method of Lung Ventilation. An increase of space in the chest is caused either by a contraction of the diaphragm, or by a raising of the anterior wall of the chest, or both. This causes inspiration. The chest is raised against gravity; and, when inhalation is complete, the weight of the chest tends to cause it to fall back to a position prepared for inspiration. In inspiration the tissues also are on a stretch and the elasticity in itself will slowly produce exhalation. Forced expiration is caused by contraction of the abdominal muscles, pulling down the anterior part of the chest and raising the intraabdominal pressure, forcing up the diaphragm.

crease the amount of his wheezing, usually on expiration. Salter[1] and others long ago observed this.

The animal *experiments of Weber*[5] are perchance of a significance equaling those of von Strübing. Asthmatic dyspnea was developed experimentally in animals. The chest became distended, the intercostal spaces bulged and there was every evidence of marked distention of the air vesicles. The condition existed whether the respiration was or was not artificial. On opening the chest, the lungs expanded promptly and under artificial respiration breathing became easy, whereas without artificial respiration the lungs collapsed. *Weber concluded that the cause of the dyspnea was change in the circulation,* and but slight, if any, spasm of the bronchial muscles. The lungs would be distended even with the chest open more than when closed if the constriction of the bronchioles were due to muscle spasm; whereas with an open chest, the expanding of the lungs allowed the circulation to become readjusted; and the congestion and edema within the bronchi disappearing, the bronchi became patent. It was shown by the work of Auer and Lewis[6] in guinea pig anaphylaxis that in definite bronchiolar muscle spasm, the lungs remained distended when removed from the chest and even when cut into many pieces.

Of equal, likely of even greater, importance than either von Strübing's or Weber's experiments are the observations of Ephraim,[7] Adams,[8] Störk,[9] Glasgow,[10] Nowotny,[11] Keiper,[12] Heilskoy and Mahler,[13] Freudenthal,[14] Möller,[15] and others that the *mucosa* of the bronchi when *seen through the bronchoscope* or laryngoscope during an attack *is* much *swollen,* usually reddish and plainly edematous. Some of these observers, notably Mahler and Heilskoy, who studied thirty cases, observed in addition that during the intervals between the attacks the mucous membrane was much more nearly normal in appearance, though usually not entirely normal. They also made the significant observation that *during* expiration, and especially during *coughing,* the *bronchi* were seen almost to *close.* Ephraim and Möller each found that the swelling and redness disappeared after an injection of adrenalin.

Shambaugh,[16] Talbot,[17] and Missildine[18] have separately observed, in what each called *anaphylactic asthma,* that *edema and swelling existed in the upper respiratory passages.* Talbot observed also that there were signs of *edema and swelling* in the *bronchi.* Campbell[19] reported a man with hay fever asthma who had the sensation that the swelling and congestion of the hay fever extended into the bronchi as the asthma developed. I have had one patient who had the same sensation.

In all cases of asthma there are evidences of *inflammation within* the *bronchi.* Some clinicians have expressed the opinion that in many cases the process in the bronchi is the result rather than the cause of asthma. But practically all, if not all clinicians concede that in many, and some that in the majority or even in all cases of asthma, the bronchitis is a forerunner of asthmatic dyspnea; and a few clinicians have arrived at the conclusion that all asthma is actually dependent upon a bronchitis preceding it.

Holt,[20] Crandall,[21] Barbarin,[22] Arkawin,[23] McClanahan,[24] Comby,[25] Hutinel,[26] and others have observed that the *asthma* of children is *usually preceded by whooping cough, measles, bronchitis or bronchopneumonia, etc.* LaFetra[27] found that 27 of 43 cases in children had had a very definite respiratory tract inflammation. Hutinel says asthma in children is always preceded by catarrhal bronchitis. It is a common occurrence, we well know, for childhood diseases to be complicated with bronchitis.

Von Strübing,[28] Dünges,[29] von Hoesslin,[30] Percepied,[31] Berkart,[32] Landouzy,[33] Goldmann,[34] Krez,[35] Hofbauer,[36] Patton,[37] Saenger,[38] Ephraim,[39] Soca,[40] McPhedran,[41] and others have commented especially upon the *frequency of bronchitis as a forerunner of asthma.* Koessler and Moody,[42] Krez,[35] Soca,[40] Saenger,[38] Stadler,[43] and others have observed in many cases that bronchial inflammation always precedes asthmatic dyspnea. Saenger calls attention to the fact that patients are *prone to forget mild attacks of "cold" and grip* even though their bronchi are affected. *Bronchial catarrh is given little attention by the average individual* unless some more or less serious complication develops. A mild bronchitis, perhaps escaping attention, but helping to develop asthma, will soon be aggravated to such an extent that there will be no doubt of its existence.

Grünbaum,[44] Babcock,[45] Carmalt-Jones,[46] and others have reported cases where certain bacteria were isolated from the sputum; *vaccines* were prepared from the bacteria found and when administered to their respective cases *frequently afforded relief.* Jones used the vaccine obtained from one case upon a large series

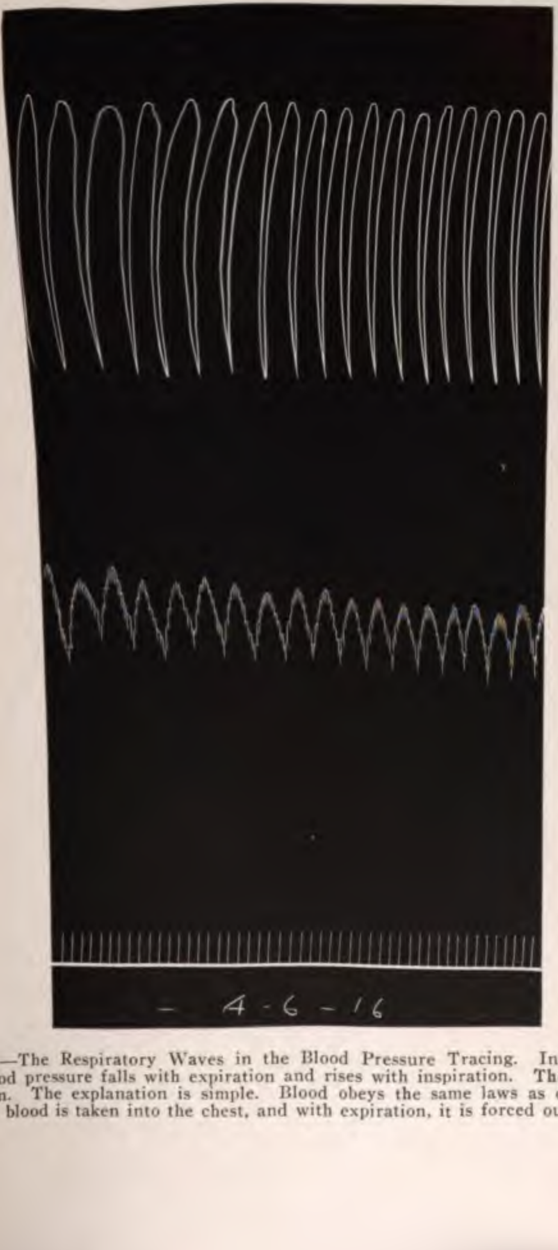

Fig. 12.—The Respiratory Waves in the Blood Pressure Tracing. In small animals, arterial blood pressure falls with expiration and rises with inspiration. The reverse is the case in man. The explanation is simple. Blood obeys the same laws as does air. With inspiration, blood is taken into the chest, and with expiration, it is forced out just as is air.

of sufferers and a fair percentage of them were greatly benefited. Comparatively numerous are the reports, particularly in the proprietary drug journals on the value of stock vaccines in asthma.

Hall[47] reports the case of a *physician* who *developed asthma following* a severe attack of *whooping cough.* Fodor[48] followed one case of asthma for ten years. *Every attack* of asthmatic dyspnea that the patient had in this time was *preceded by an acute exacerbation of bronchitis.*

Goldmann[34] observed in his asthmatic cases that there was commonly an *infected focus* somewhere *in* the *upper respiratory passage*—in gums, tonsils, nose, etc.—and that there *also* was *a bronchitis,* which he believes was secondary to the upper respiratory tract processes.

Landouzy,[33] Krez,[35] Soca,[40] and others are of the firm conviction that the *bronchial catarrh* of asthma *hinges upon* a chronic latent *tuberculous process* in the lungs. Cabot[49] holds that the diagnosis of chronic bronchitis should usually be tuberculosis instead, which is to say that the former is dependent upon the latter.

Tauszk[50] claims that there is a special type of tuberculosis which is prone to develop asthma. While formerly it was held that *asthma and tuberculosis* were incompatible, there have been in the last few years so many reports where the two existed together that there are probably very few who will not admit that they *may at least coexist* and may possibly be interdependent.

Abbott,[51] Thompson,[52] Saenger,[38] and von Strübing[28] have commented especially upon the significant part *cough* seemed to play in developing the asthmatic paroxysms. West[53] in a study of the respiratory changes *in hemiplegia,* made the following observations: "Coughing produced the most extraordinary effect, for while the sound side contracted, the *paralyzed side bulged or was blown out.*" This evidences the high intravesicular air tension developed by sudden forceful expirations.

Patton[54] reported a case of asthma presumably reflex to *buried tonsils.* In describing the development of the attack he says it came on after ten minutes of very *vigorous sneezing and coughing;* the paroxysm was set up by touching the tonsils. Removal of the tonsils cured the case. Missildine[18] reported some experimental work with horse serum. Spraying it in a 1-700 dilution of normal saline on the Schneiderian membrane set up a *paroxysm of* *coughing and sneezing which was followed by asthmatic dyspnea.* Further evidence as to the importance of bronchitis, bad "colds," tuberculosis, coughing, sneezing, etc., will be found in later chapters.

As to the part played by overfilling of the veins because of the *horizontal position,* numerous clinicians bear testimony. Worthy,[55] Abbott,[51] and Ephraim[39] are among those who have particularly commented on the frequent occurrence of attacks while the patients are in the horizontal position.

I regard of extreme value in supporting my contentions the numerous observations by clinicians that the attacks of asthmatic dyspnea are partially, if not completely, relieved by almost any sort of treatment which tends to make the sufferer expire slowly with little or no muscular effort. It is probable, I hold, that the reputed *value of the various inhalants, smoking powders, cigarettes, etc., lies in the fact that they cause the patient to make slow expirations* in order to hold the medicament longer in contact with the bronchial mucosa.

To the same factor, I repeat, is doubtless due the good which some patients get from *smoking* a cigarette or a cigar, *blowing* a mouth harp, etc. I once had a nurse in my employ who suffered from asthma and she obtained relief from smoking cigars. Others have reported similar instances. Imagine an individual enjoying a good cigar or taking a *medicament by inhalation* and not giving a liberal period for expiration.

Saenger,[56] Kuhn,[57] von Strübing,[28] Avellis,[58] Hofbauer,[36] Stadler,[43] and others have found that *respiratory drills* in which slow passive expiration was insisted upon, were of inestimable value in relieving asthma. Some even claim that a month or so of such regular drill will permanently cure the disease.

Staehelin and Schütze[59] have observed, as have many others, that any slight distress in *breathing* tends to cause it to become a *subjective* factor; when this occurs, expiration as well as inspiration is made with forceful muscular effort.

Williams[60] and Laennec[61] each long ago observed that if a patient suffering from asthma held his breath for a few seconds, he was then able to take one or two quite normal breaths, "as if by magic." Einthoven[62] noted that if a *patient breathes easily,* his *paroxysms will leave* him.

All clinical writers on asthma refer to the *piping, whistling râles* which are diagnostic of asthma. These râles are *made in the moderate sized tubes*—in those certainly over 1.0 mm. in diameter—*which have considerable cartilage and fibrous tissue in* their *walls* and hence will not collapse from the intrapulmonic pressure which is produced by forceful expirations. It is in this portion of the tubes that the *congestion occurs* especially. Here there are *mucous glands* which congestion will stimulate to *secrete*. The *mucus* helps to *block* the *tubes* and hence contributes toward causing both the sounds and difficult breathing of asthma. The mucus has a tendency to form into pellets. Berkart[32] is convinced that the pellets obstruct the passages so as to cause dyspnea. He has made an exhaustive study of the subject.

As bronchitis and irritation of the bronchial mucosa may be localized in certain parts of the lung, so may *asthma* be *localized*. Berkart[32] and Hoover and Taylor,[63] and others reported instances of this. I have seen one case where the findings existed in a part of the lung only, and which were for the most part objective rather than subjective.

The *sputum findings* and the condition of the bronchi at autopsy is supportive evidence that a bronchitis, often very mild, practically always exists in asthma. This is discussed more extensively in the chapter on pathology.

The majority of the clinical writers on asthma have been divided between the theory of muscle spasm and that of vessel turgescence. It was first suggested by von Strümpell[64] that the failure to find hypertrophy of the bronchiolar muscle of asthmatic subjects at autopsy was very strong negative evidence of the bronchiolar muscle spasm theory. The fact that the majority of clinicians have been divided between these two theories causes me to say that the *lack of* evidence of a *hypertrophy of the bronchiolar muscle* in asthmatics is therefore *positive evidence for the vessel turgescence theory.*

The nonpassive expiration theory helps to *correlate* a great number of the various *theories* which have been advanced to explain asthma and harmonizes and clarifies many of the observations which have been made as to the nature of this disease or affliction. There is much evidence in other chapters, notably in Chapter III, which properly belongs in this, but the force of it will doubtless be enhanced by lack of repetition.

Even if the *bronchiolar muscle* may become tonically contracted by anaphylactic or other stimulation and thus set up a dyspnea, there must ultimately result the mechanical disturbance of the circulation of the lungs and bronchi.

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# CHAPTER XII.

## THE SPASMODIC CHARACTER OF ASTHMA.

An occasional writer lays great stress upon the spasmodic element in asthma indicating that in some cases there is little or nothing else of any moment. There is also a tendency it seems, for a few clinicians not to label as *"pure spasmodic"* asthma those types of the condition in which evidence is found of definite inflammatory changes within the bronchi. Even those writers, however, who refer to "pure nervous spasmodic" asthma, when detailing case histories, invariably give such facts as prove catarrhal involvement of some grade of the respiratory passages.

As a rule the assumption has been that the coming on of the attack in an individual apparently in good health, as well as the *suddenness* of its *appearance* could only be explained on the basis of spasm of the bronchiolar muscle fibers. I am of the opinion first, that asthma does not come suddenly on an individual while in a good state of health; and secondly, that most attacks come on gradually rather than suddenly; and thirdly, that it is not necessary to assume that the muscle fibers of the bronchioles have any part in the production of the attack.

The first spell of asthma that an individual has comes usually after months or even years of respiratory tract infection. The older generation was not instructed in the significance of protracted *"colds" and coughs* and, of course, gave little heed to them. Therefore, when asthma supervened upon the chronic bronchitis or other catarrhal condition, our ancestors thought only of the terrifying distress of breathing. This doubtless accounts for many of the instances where it was assumed that the asthma "came like a stroke of lightning from the clear sky."

After the first attack is once produced, the *subsequent attacks* may come more easily and quickly; that is, the more attacks one has had, the more readily and easily they develop.

The strain that prolonged nonpassive expiration throws upon the *blood vessels* of the bronchi causes them to *dilate* and swell the mucosa so as to fill the lumen of the bronchi. When this state is once produced, it is brought on more easily the second time and each subsequent attack becomes still easier.

While usually markedly inflammatory conditions of the bronchi plus prolonged paroxysms of coughing are necessary to bring on the first attack of asthma, later the mere fear of an attack, anger, excitement of any sort, or a very slight "cold" may be sufficient to precipitate it. Or again, the *inauguration of* the *attack* may be due to a sudden hyperemia of the nose causing altered respiratory efforts, or it may be a dyspnea from exercise, acidosis, nephritis, cardiac decompensation, aneurysm, enlarged bronchial lymph nodes, overfilling of the stomach, gas in the intestines, pain, etc., etc.

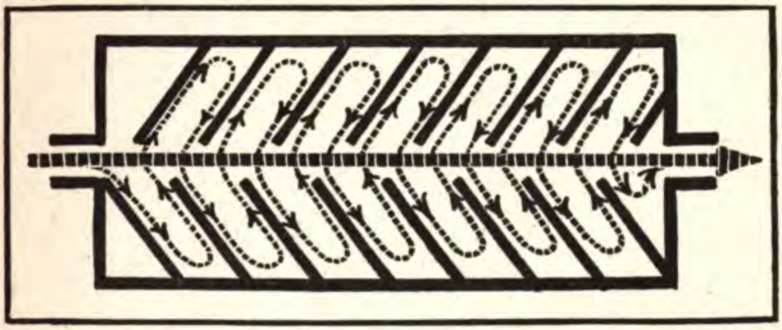

Fig. 13.—The "Muffler." This illustration is of a Maxim Silencer, but the principle of a muffler is identical. Various constructions have been used for mufflers. The essential factor is that there are many blind pockets. Air passing through the muffler under high momentum will have the momentum greatly reduced, whereas with a low momentum, its momentum will be reduced but little.

The breathing is affected by such a large *number of factors;* and any alteration of the breathing is likely to cause muscular effort on expiration, and hence may be responsible for an asthmatic attack. The many causes that are known to have been connected at one time or another with the production of asthmatic attacks, I think are explainable on this basis.

*Attacks* commonly come on *at night,* usually around three o'clock in the morning. My explanation of these attacks is that the circulation is at a lower ebb around this hour, the large veins are distended by the horizontal position and blood is dammed to the bronchial veins and capillaries causing a swelling of the mucosa, and possibly some hindrance to the passage of air through the tubes. From this comes dyspnea, nonpassive expiration, and asthma. A second important factor is that the horizontal position allows mucous material in the bronchi to accumulate in the trachea. This finally reaches a location in the upper trachea where it causes coughing—not only this, but also labored breathing. This may go on some time before the individual awakes, so that the attack is well started before consciousness arrives. The sensation of dyspnea, choking, and an inability to get air comes on while the patient is in a semiconscious state, and he awakens in a fright. This, plus forceful coughing which he is likely to have on waking, precipitates the attack in earnest.

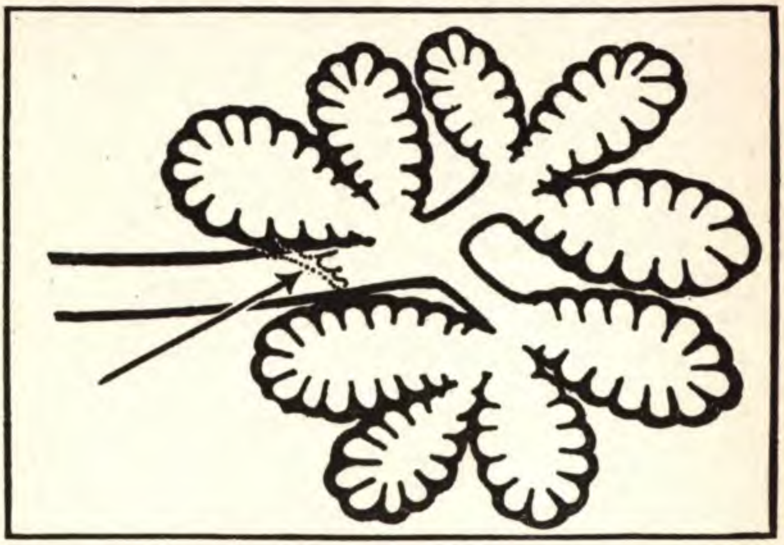

Fig. 14.—Schematic Cross Section of the Lobule-"Muffler" Construction of a Lobule. There is a striking similarity in the construction of a lobule and that of a muffler. The lobule is much more complicated in construction as the above drawing indicates; this may be seen by referring to Fig. 3. Air leaving the alveoli, if under high momentum of a forced expiration, will have its momentum greatly reduced before the bronchiole is reached just as happens in a gasoline motor muffler. The point indicated by the arrow shows how a flap of a dividing wall within the lobule might act as a "trap" or "valve," seriously obstructing the egress of air. Again the infundibula may have air tension so greatly increased that their pressure upon the side walls of the bronchiole may be sufficient to partially collapse it.

Sometimes patients get to *expecting an attack* at a certain hour of the day. In such an event, the labored breathing begins as a psychic affair and induces the real asthma. A physician friend of mine informed me that his sister has been a sufferer from asthma for years. At times the attacks have been so distressing that she was opposed to allowing him to leave the house. When it became obligatory for him to leave she extracted each time a promise that he would return at a definite hour. Invariably he would return at the appointed time only to find her rapidly developing an attack of asthma. Ultimately he concluded that it was best to find it impossible to know when he could return and in this way he prevented many attacks for her. The onset of her attack after that was liable to be with his approach.

It seems possible that in rare instances the first attack of anaphylaxis or of an *angioneurotic edema* affecting the bronchial mucosa might be of such a grade as to produce an extremely severe dyspnea. If this were then accompanied for some time with very forceful expirations, asthma would be sure to supervene. If, however, there had been many previous attacks of a moderate grade of hyperemia with forceful expirations for protracted periods, then an attack of anaphylaxis or angioneurotic edema with an unusually severe grade of swelling of the mucosa, producing a simple dyspnea, perhaps even with little or no coughing or sneezing, would surely and promptly produce asthma.

Since mildly *inflammatory conditions* of the bronchi even with a moderately severe grade of coughing are prone to *pass unnoticed* or to be soon forgotten, it is not surprising that in some instances the first attack of asthma seems to have arrived suddenly without admonition or preparation.

Asthma depends upon a widening of the fine blood and lymph vessels of the mucosa and other tissues lining the bronchi, and hence long periods of forceful expiration will usually be required to bring on the *potentially asthmatic condition.* But after this is developed, subsequent attacks may arise with a comparatively small amount of nonpassive expiration.

# CHAPTER XIII.

## THE EXCITING CAUSES OF ASTHMA.

A large number of persons have *inflammation* of parts of the *respiratory tract* for variable periods, especially during the seasons when the weather is most changeable, and the bronchi are likely to become involved. Children are prone, early in life to develop infections of the throat and chest. Fortunate is the babe with a grip or "bad cold" who does not also have the bronchi involved.

Certain children are by virtue of heredity and surroundings or both, more predisposed to these infections than are others. After one or two or more winters of "*colds,*" *grip,* bronchitis, and cough, there come along *measles* and *whooping cough,* first one and then the other, and while there may be no alarming symptoms as regards life, the cough may become chronic and the bronchitis continues, sometimes nearly well, sometimes mild, and occasionally more or less severe.

After a time the child or adult, as the case may be, may cough till he "loses his breath;" then later he may have attacks of shortness of breath—dyspnea—following the *coughing spells* and eventually the dyspnea may become of the asthmatic type. Such an individual may have periods of entire or comparative freedom from the affection, but there is ever the danger that when once started, the condition will tend to become chronic. As it has little likelihood of ending life, the individual becomes a confirmed asthmatic.

As the children of asthmatics may have the *hereditary factors* which predispose to respiratory tract infections and also the environment to help along, asthma in such cases is to all intents and purposes a hereditary disease.

Not the least important of the causative factors of asthma then, is the *belief* of many parents and lay people generally that "*colds" and coughs* are necessary and *unavoidable* incidents in the life of every individual and hence need receive but little or no consideration.

As a child develops infections of the respiratory passages which tend to become chronic, so may an adult. We all know the clinical history of these cases of *chronic* respiratory tract *infections*. They are too common to require detailing here.

The fact that these *conditions* are *so common* is the only reason that I can assign for the many failures of those who have studied asthma closely to recognize the relation of them to asthma.

*Very few indeed are those who have considered the type of breathing in asthma even to be of significance from the etiologic standpoint. Thompson,*[1] in his book on Clinical Medicine, says, "The majority of cases of asthma are caused by an interruption in the act of expiration from coughing," and emphasizes that the hard coughing may arise from any cause.

*Von Strümpell*[2] writes, "Not infrequently asthmatic attacks are combined with a permanent inflammatory and catarrhal condition of the finer bronchi," and "Previous attacks of acute bronchitis must be especially taken into consideration," and again, "Some cases are referable to a severe bronchitis complicating measles or whooping cough during childhood." Von Strümpell, however, apparently does not recognize the significant part played by coughing. *Anders*[3] notes that at autopsy the findings peculiar to bronchitis are present but says nothing about bronchitis and cough playing an etiologic role.

*Osler*[4] says, "Asthma attacks may follow whooping cough," and again, "Chronic cases in which the attacks recur year after year, gradually become associated with emphysema, and every fresh 'cold' induces a paroxysm." This is the nearest he comes to discussing bronchitis and coughing in relation to asthma. *Dieulafoy*[5] thinks, "In most cases they are complicated by a catarrhal element of variable intensity," and again, "In some asthmatics the fever, the cough, and the nature of the spasm prove that bronchitis is present."

*Most authors* refer to the frequent concomitancy of asthma, and bronchitis and coughing, but in the main, the bronchitis is considered only as an unimportant factor in the etiology of asthma. The cough is frequently mentioned but usually no importance is attached to it. Saenger,[6] Thompson,[1] Abbott,[7] and von Strübing,[8] are the only authors I have read who seem to attribute the importance to cough that I hold should be given to it.

Nonpassive expiration unassisted by some inflammation of the bronchi will rarely produce the asthmatic state; the *character of* the *infection,* however, will have a modifying action upon its production. An inflammatory state of the mucosa may be so marked as to produce dyspnea without having set up coughing at all. Then simple dyspneic breathing coupled with the inflammation may promptly bring on an asthmatic attack. This might happen in an anaphylactic reaction, an angioneurotic edema, or similar conditions affecting the bronchial mucosa.

Or perhaps, it must be admitted, some split protein or other toxin in the blood may bring on tetanus of the muscle of the bronchioles which in turn causes labored breathing and the circulatory changes in the mucosa necessary to asthma. My experience and a thorough study of the literature convinces me that even in most cases of *"hay" asthma* there exists first, for a variable number of seasons, the redness, swelling and irritation of the nose, pharynx, and trachea, coupled with the sneezing. Gradually the bronchi become involved, coughing is added to sneezing, wheezing and dyspnea appear, and finally asthma.

As *not all* who cough with great force, or who have severe simple dyspnea *develop asthmatic dyspnea,* some explanation should be offered therefor. Whether the forceful expiration produces asthma will depend upon several factors; namely, (1) the force, the duration, and the repetitions of the forceful expirations; (2) the strength of the walls of the vessels in the bronchial mucosa; (3) the extent, character, and severity of the bronchitis; (4) the strength of the right heart, or its ability to withstand the increased pulmonary blood pressure; (5) the natural resistance and resilience of the tissues; and (6) the extent to which the expiration collapses or flattens the thin-walled bronchioles.

Some patients cough violently, each *cough* beginning precipitately and with all the force that can be applied by the strong expiratory abdominal muscles, and this may continue, each cough followed by another with extremely short intermissions for inspiration until the paroxysm ceases because of *exhaustion.* Or, a patient may restrain himself so that each act of coughing is initiated less precipitately and longer intervals taken for inspiration, allowing the paroxysm gradually to subside before a state of exhaustion ensues. The greater the force and duration of the expiration, other factors being equal, the greater is the likelihood that the dilation of the vessels of the mucosa will be sufficient to cause asthma.

The degree of *dilatation of* the *blood and lymph vessels* of the mucosa will depend, in addition to the grade of intraalveolar pressure applied to the bronchial vein, upon the strength of the walls of the vessels, i. e., the resistance they have to stretching. Some persons develop varicosities and dilatation of venules much more readily than do others as is evidenced by the findings in the legs, scrotum, etc., of different individuals.

The presence of *bronchitis* for years and even months will certainly *weaken* the walls of the *vessels,* thus tending to allow distention and edema. In case the bronchitis begins in early childhood years and continues into adult life, the possibility of the development of asthma is increased. In some patients the vessels of the mucosa may stretch readily but there may also be a high grade of resilience, a strong tendency to return to normal states.

If the *right heart* is *weakened* the damming of the blood into the larger veins, the bronchial veins, and mucosa capillaries will be facilitated. The extent to which the suddenly increased intraalveolar pressure causes collapse of the walls will depend upon the rigidity and caliber of the walls of the finer tubes. And it is not difficult for us to assume that these walls vary in different individuals the same as other structures vary.

*Sneezing* is the same sort of an expiration as coughing and it would seem reasonable that in some cases at least, sneezing might be the chief etiologic factor in inducing asthmatic dyspnea. It certainly may cause the precipitation of an attack in one who has a well developed asthmatic condition. That sneezing in the absence of bronchitis may be responsible for asthma I feel disposed to doubt, unless it is long continued and intense. But the condition which is responsible for sneezing may be also responsible for changes in the bronchial mucosa and may be so mild as to escape detection.

*Excitement* and *physical exertion* of sufficient degree to accelerate the breathing and make it labored may so increase the intraalveolar pressure as to cause the development of asthma in an individual who already has the asthmatic condition; or even the *psychic state* may inaugurate the application of force to expiration actually causing a sufficient damming of the blood and lymph into the mucosa vessels to obstruct expiration.

*Odors, dust, or irritants* of any sort may act by inducing rapid labored breathing, coughing or sneezing, and in this way cause an asthmatic attack.

The *position* of the patient is a factor of some importance. The longer one lies at absolute rest, the lower becomes his circulation and if in a horizontal position, the more the blood accumulates in the larger veins; hence the greater is the damming of the blood into the bronchial mucosa.

Fig. 15.—Box and Marble. The experiment is performed by moving the box rapidly to and fro in a horizontal position in the direction of the long axis of the box; while the box is thus moving, a marble is dropped into it about midway between the ends. The result is shown in the next figure.

Then, too, the individual with a bronchitis usually has *excretions in* the *bronchi* which accumulate in the upper respiratory tract especially after he has been lying on his back for a few hours. These may induce a coughing spell which, plus the congestion brought on by position, causes the culmination of the attack. Or the accumulation of mucus in the upper part of the trachea may

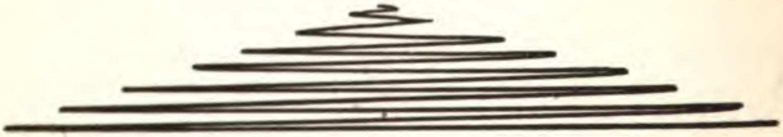

Fig. 16.—The Course of the Marble. As the box moves first in one direction and then in the other, the marble begins to roll in one direction and then in the other with the movement of the box, increasing the distance and momentum with each oscillatory movement of the box. After a few moments, the marble is going from one end of the box to the other with each movement; the rebound the marble obtains by striking the ends of the box adds to its momentum.

reflexly cause the breathing to be so altered even while the patient is yet asleep that when he awakens the attack is fairly well started.

The part played by the general mental attitude and the *habit* of being frightened at the impending attack must not be overlooked. This, together with the filled vena cava and distended right heart, may be responsible for many attacks. *Fright* causes the individual to begin frequent and labored breathing, the intraalveolar pressure grows, and soon the spell is on.

A *full stomach* may be responsible for attacks of asthma in one who is asthmatic because it brings on simple dyspnea or because it interferes sufficiently with breathing to cause it to become a matter of attention from the conscious mind; in voluntary breathing force is naturally applied to both phases.

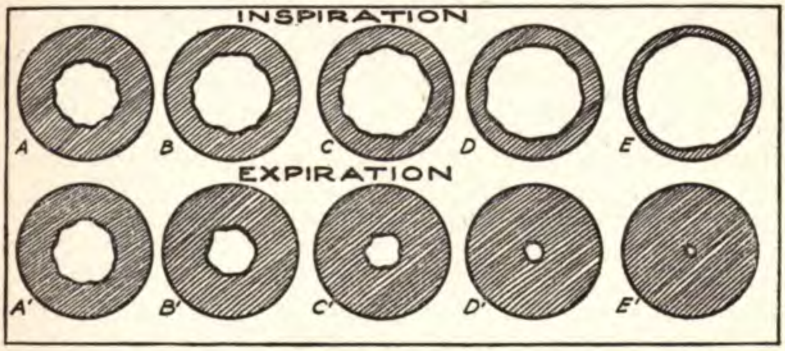

Fig. 17.—Simple Dyspnea Changed to Expiratory Dyspnea. Just as it takes time for the marble's excursions to reach the maximum, so after dyspnea starts, the blood and lymph during expiration are forced into the bronchial vessels and spaces and from there into the chest, slowly at first, putting the lymph- and blood-containing walls on a low tension: with much forced inspiration and expiration rapid oscillation of the fluid is developed. Like the marble rebounding after striking the wall of the box, a high tension within the vessels of the bronchi helps to send the fluid into the chest with inspiration. The tension developed within the chest vessels during inspiration helps during expiration to force the fluid to the bronchial spaces and other vessels outside the chest. Thus the harder and more forceful are both inspiration and expiration, the easier becomes inspiration and the more difficult becomes expiration.

An asthmatic with gall-bladder disease, appendicitis, stomach ulcer, pyosalpinx, neuralgia, or other affections, may suffer pain, distress, or worry which may unconsciously to him set up a type of breathing in which expiration becomes nonpassive. Or these infective processes may have exacerbations which may secondarily affect the process in the bronchi and thus be responsible for an attack of asthmatic dyspnea. So in reality there are many *reflex causes* of asthma.

From what has been said it can be seen what *a variety* of things may contribute to the attacks in different individuals. What is responsible for a precipitation of the paroxysm in one may not affect another.

With hay fever and other *anaphylactic states* there is always more or less inflammation and blood vessel engorgement which may extend well into the bronchi. The same may be said of inflammatory conditions of the nose, sinuses, tonsils, teeth, etc. Anaphylaxis, tuberculosis, and the nose in their relation to asthma will be discussed more fully in subsequent chapters.

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# CHAPTER XIV.

## BRONCHIAL MUSCLE SPASM THEORY.

Of the two main theories—the one of bronchial muscle spasm and the other of vessel turgescence—which have held sway for a half century or more, the conception advanced in this monograph is in the main a support and interpretation of the latter; but the former has been a popular theory in the minds of many and is not to be promptly dismissed as being of no further use.

From what I can learn, it seems that the *strongest support* for the bronchial muscle spasm theory has been that first, the *lungs have the power of contracting* as was first shown by Williams[1] and others, by passing a current of electricity through them; second, it has been conclusively proved that the finer bronchioles have walls relatively rich in smooth muscle fibers; third, the fibers may be stimulated through the vagi to contract; and fourth, no other theory has seemed to explain the facts as well as this.

It was Aufrecht[2] who worked out the arrangement of the bronchiolar muscle fibers; and Gerlach,[3] Horvath,[4] Einthoven,[5] Brodie and Dixon,[6] and Beer,[7] who proved that *stimulation of the vagi* caused the muscle fibers to contract. Since the time of Cullen,[8] who probably originated this theory in the last half of the eighteenth century, there have been many who argued loud and long in support of the theory, but *few to add actual evidence* in its favor.

Jackson,[9] however, by an ingenious device, has been able to present *new evidence on the ability of the muscle to contract.* He makes an incision in the chest wall of an anesthetized animal, inserting an apparatus which holds the chest rigid and expanded: the chest is then closed air tight. Engaged with the apparatus are two tubes, one for admitting air into the pleural space and the other for withdrawing it. By this means a *new form of artificial respiration* can be carried on. In Jackson's experiment the animals are decerebrized by means of a probe inserted in trephine holes, thus preventing natural breathing. Alternate aspirating and admitting air from and to the pleural spaces effects respiration. Inspiration results from the negative pressure in the pleural spaces the same as does natural inhalation, and expiration comes from the elasticity of the tissues as does normal passive exhalation. But the expiratory forces in his experiments are weaker than under normal conditions: the immobilization of the chest does away with the influence of gravity and the elasticity of the tissues of the chest walls, both of which help normal exhalation. By means of a tambour connected to a side arm of the tracheal cannula, the vibration of the air in the trachea can be registered.

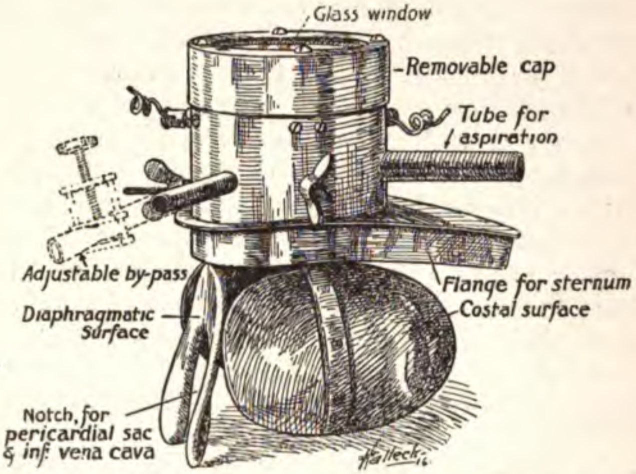

Fig. 18.—Jackson's Instrument for Artificial Respiration. In an anesthetized animal, the skin, sternum, and pleura are divided in the median line. The instrument is introduced into the chest. The side wings are adjusted so as to fix the chest walls rigid and the lower O-shaped plate placed to hold the diaphragm firm. The skin is drawn and sewed about the triangular flange. An aspirating apparatus is attached to one of the side tubes; this produces inspiration. Air enters the pleural cavity through the other side tube, and the contracting power of the tissue effects expiration. This ingenious instrument is described in detail by Jackson. (From Jackson: Experimental Pharmacology.)

Jackson has shown that certain drugs, notably arecoline, when injected in large dosage, sufficient to stop the heart's contraction, cause a marked reduction in the oscillation of the air in the trachea. This interpreted, means that *arecoline stimulates the bronchial muscle to contract. Atropin,* which paralyzes the endings of the bronchoconstrictor and heart inhibitor nerves, when injected into the animal, promptly *overcomes the bronchial muscle spasm* and admits the passage of such an amount of air that the currents in

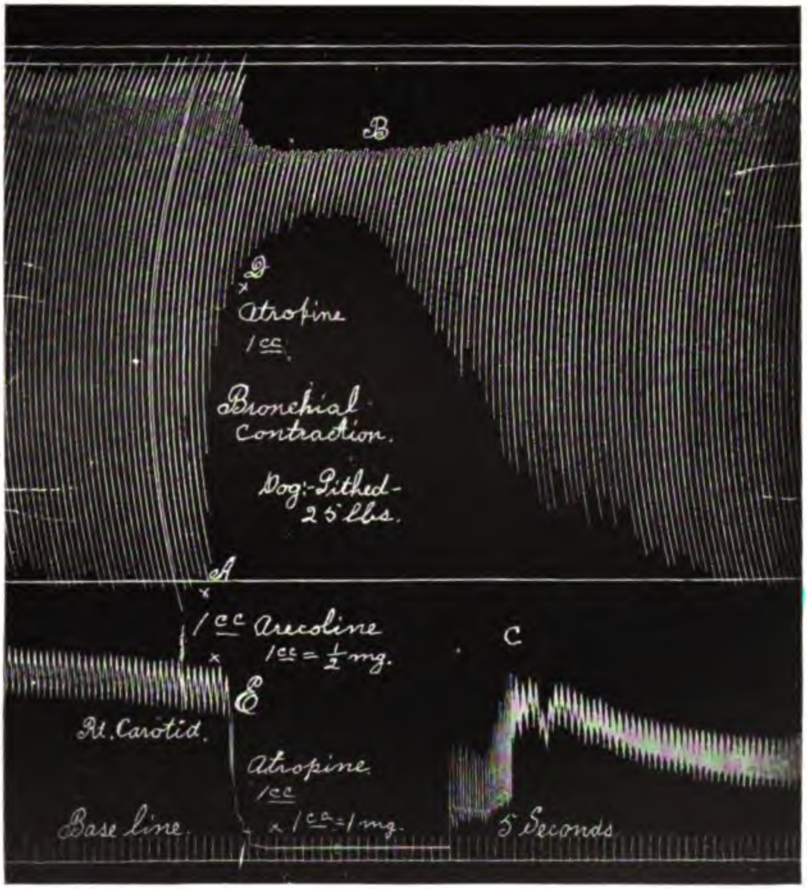

Fig. 19.—Bronchotetany (A Possible Indirect Cause of Asthma). By means of his instrument, Jackson has been able to show clearly that certain drugs produce bronchiolar constriction through stimulation of the constrictor nerve fibers. This is shown beautifully in the upper tracing. One c.c. arecoline injected intravenously at *A* produced serious narrowing of the bronchiolar lumen at *D*. It is interesting too, to observe by the lower tracing that the dose of arecoline was sufficient to cause the heart to cease activity. Atropin, which paralyzes nerve endings, was introduced at *D*, and it allowed the bronchodilator nerve fibers to cause widening of the bronchi, beginning at *B*. (Courtesy of Dr. D. E. Jackson.)

the trachea become normal again. This shows that the muscle contraction produced by *arecoline* in the blood is by virtue of an *influence upon nerve tissue.*

In the same animal and immediately following the above experiment, *dionin* is injected and a reduction occurs in the amount of air passing to and from the lungs. We must conclude that dionin *acts* directly *upon the muscle* because the nerve was put completely out of function by atropin. *Adrenalin overcomes the effect of dionin.*

Jackson argues on the basis of these experiments that there *may be two types of bronchial asthma,* one from substances which *affect* the bronchial muscles *through* the *bronchoconstrictor nerves* and which should be relieved best by atropin, *and* a second from substances which affect the bronchial *muscle direct* and which should be relieved by adrenalin.

The author says, however, that *among the many drugs which produce direct muscle spasm are most of the opium alkaloids,* morphin, heroin, codein, etc. I believe this at once supplies convincing evidence that clinical bronchial asthma is not essentially a spastic contraction of bronchial muscles, for *morphin and codéin* are the very agents which up to the advent of adrenalin were the drugs most *commonly used to relieve asthma.*

*In the tracings* presented by Jackson, the up stroke is made by expiration and both tracings indicate that *expiration is more complete than inspiration* during the periods of muscle spasm. That is to say the narrowed part of the tracings are located near the position of extreme expiration. On first thought it might seem that this meant that bronchial muscle spasm allowed expiration more easily than it allowed inspiration. But this is not the case. The interpretation, as I see it, is: the force of the elastic tissues of the lung is greater than that the experimenter used to produce aspiration of the pleural spaces. By using greater power to suction air from the pleural cavity, an emphysemic condition of the chest would certainly be produced.

To make this experiment complete, it would be necessary to have the aspirating force exactly equal to the power of the inspiratory muscles of the animal and in addition to the expiratory force of the elastic tissues there should be a force commensurate with the power of the expiratory muscles of the animal. *If, with these* *forces as in a normal animal, emphysema developed and the dyspnea became chiefly expiratory; if mucus were excreted and casts, spirals, etc., formed; if typical whistling râles resulted and there were no circulatory changes; then and then only, I believe, could asthma be truly declared the direct consequence of bronchial muscle spasm.*

This question of *what action of the muscle makes expiration more difficult than inspiration* has been repeatedly asked and not satisfactorily answered, and it should be answered before accepting the spasm of the bronchiolar muscle fibers as being the essential factor in the production of asthma. The explanation of Watson-Williams[10] is not sufficient, for it simply leads us to ask two questions which remain unanswered; namely, why does the contraction become excessive in expiration, and do the fibers actually dilate with inspiration? The theories offered by Grant,[11] by Brodie and Dixon,[6] and others are also inadequate.

It has been significantly asked, "*Are the muscle fibers of the bronchi strong enough* to remain in a state of active tonic contraction for hours or days at a time?" Brodie and Dixon found that the *fibers soon fatigued* on electrical stimulation. Paul Bert[12] and Williams[1] each found the *muscle* to be very *weak*. With the lungs fully distended with air the muscle failed to contract from stimuli applied to the vagi. But when much air was let out of the lungs, the muscle was able to effect a contraction on stimulation of the nerves.

Then, too, as has been said in a previous chapter, the *muscle* of the bronchioles has *not been found* at autopsy of asthmatic subjects to be *hypertrophied.*

The *whistling râles* of asthma *indicate* positive *involvement,* especially *of the tubes of medium size.* The absence of an overwhelming number of very fine râles at least in the immediate onset of the attack goes far toward disproving the bronchial muscle spasm theory.

The development of our knowledge of *anaphylaxis,* especially as regards the lung manifestations in guinea pigs has led many to assume that asthma is the result of anaphylactic shock and that this is because of the effect of the protein on the bronchial muscle. This will be discussed more fully in the next chapter.

If contraction of the bronchial muscles should occur, it probably

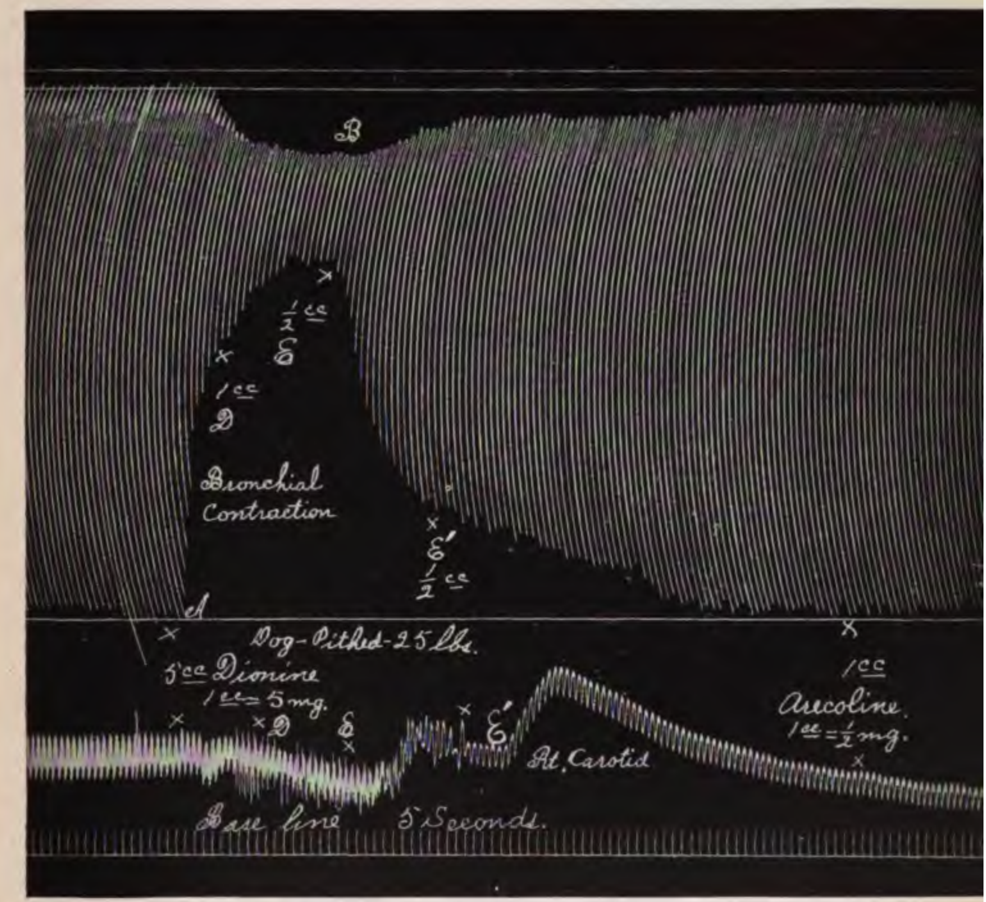

Fig. 20.—Bronchotetany (A Possible Indirect Cause of Asthma). Certain drugs act on the bronchioles by affecting the muscle tissue. After the tracing in the preceding illustration was obtained, for which the nerve endings of the bronchioles had been paralyzed, 25 mg. of dionin were injected at *A*. This produced contraction of the bronchiolar muscle by direct effect upon the muscle. An injection of atropin at this juncture made no change. Adrenalin, however, introduced at *E* and again *E′* produced complete dilatation of the bronchioles. (Courtesy of Dr. D. E. Jackson.)

would interfere to the same extent with inspiration as with expiration and it would certainly bring on secondary change in the blood supply of the bronchi the same as will any other cause of labored breathing; when this condition has developed sufficiently, the expiration will become more difficult than inspiration. I suggest the use of the word "bronchotetany" as applied by Lederer for the conditions resulting directly from spasticity of bronchiolar muscle—the terms "asthma" or "bronchial asthma" to be applied only after the secondary changes in circulation have resulted.

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# CHAPTER XV.

## ANAPHYLAXIS AND ASTHMA.

A decade ago or thereabout, Gillette,[1] Kitzmiller,[2] and others, found that asthma was *relieved after diphtheria antitoxin* had been given. This caused many to use the antitoxin for the treatment of asthma. The results were inconsistent. Some patients were greatly improved, but some fatalities resulted.

The idea gradually developed that a connection existed between what was known as serum disease and asthma. Since the work of Gay and Southard,[3] Auer and Lewis,[4] Anderson and Rosenau,[5] Anderson and Schultz,[6] Biedl and Kraus,[7] Meltzer,[8] and others on anaphylaxis, and the discovery that animals, especially *guinea pigs, died in anaphylactic shock with a marked distention of the lungs* and an inability to get air into or out of them, that the condition of the lungs was not due to an edema or other circulatory changes, and that there was strong evidence of a marked contraction of the bronchiolar muscles, the old theory of bronchiolar muscle spasm took on new life. The *anaphylactic theory became* the *copartner* of the *muscle spasm theory* and many have been inclined to accept the idea that all asthma is a manifestation of anaphylaxis.

A study of the development of an *anaphylactic reaction in man,* however, shows that it *does not compare* accurately *with that in the guinea pig.* Anderson and Rosenau[5] say in regard to anaphylaxis, "The reactions in man and the guinea pig, however, differ both in severity and in kind." An extremely small second injection of a protein in a guinea pig invariably affects the lungs, whereas in man a considerable amount of protein to which he is sensitized may be given in most instances with little or no apparent effect on the respiratory system, save to quicken breathing.

Jordan[9] and Schultz[10] each working upon the histologic structures of the lung of the guinea pig to determine the cause of anaphylactic death, discovered a very pronounced *segmented* condition of the muscle of the *pulmonary arteries.* Such a condition had first been described by Piana[11] in the pulmonary arteries of certain mammals. *In the guinea pig,* Jordan found that the muscle is relatively thick and consists of circularly disposed segments of smooth muscle fibers; the spaces between the segments, being short and spanned by a thin band of smooth muscle, cause the arterioles to resemble a string of beads. Quoting from Jordan, "It is also an interesting fact that as far as has been fully tested, acute anaphylactic death cannot be produced in the animals that lack this condition (i.e., dog, cat, rabbit, mouse,) whereas, sensitized guinea pigs which possess it in an extreme degree of development succumb (by asphyxia) to a proper second injection of horse serum in from three to five minutes." The pulmonary arteries of man, according to Jordan, have the same construction as have his other arteries; i.e., they are not like those of the mammals susceptible to anaphylactic death.

It is known at least, that *not all* persons *who develop* a state of *anaphylaxis develop asthmatic dyspnea.* To illustrate, an individual given tuberculin subcutaneously for diagnosis may react violently but he does not ordinarily develop asthma. Babcock[12] and others hold that asthma may be an anaphylactic reaction to certain bacterial proteins. Yet they give autogenous vaccines, supposedly the very proteins causing the anaphylaxis, and an attack of asthma does not follow. If the reasoning by analogy holds in one instance it should in another. If man's bronchiolar muscle reacts the same as the guinea pig's to the second injection of protein, a relatively small dose should set up the spasm in man just as in the pig.

Patton[13] reports that he gave intravenously 14 injections of *phylacogen* to a patient with asthma; the usually *severe reactions* occurred but *nothing* is *said of an attack* being induced thereby. Kitzmiller[2] reported that he took an injection of diphtheria *antitoxin for asthma* and that though he promptly developed a severe serum reaction, *no asthmatic attack occurred* for three months. These experiences would indicate that asthma is only indirectly dependent upon anaphylactic reactions.

Gillette[1] obtained information of *23 individuals* who had been *given* the diphtheria *antitoxin* and had *either died or* only *developed alarming symptoms* of death. Sixteen of the 23 had histories of having previously suffered from some form of respiratory disturbance, probably asthma; 6 of the 16 died and the other 10 went into a state of collapse with final recovery. Of the seven with no history of respiratory disturbance, four died and three recovered after a serious state of collapse. Gillette draws the conclusion that it is more dangerous to give the diphtheria antitoxin to people with asthma than to those without it. This conclusion perhaps should not be disputed in the present state of our knowledge of anaphylactic shock; but it may be remarked that there was a *higher death rate among the nonasthmatics than among the asthmatics*—62½ per cent of the asthmatics having recovered and only 42⁶⁄₇ per cent of the nonasthmatics. These statistics are from such a small number of cases, however, that positive conclusions in either direction should not be drawn.

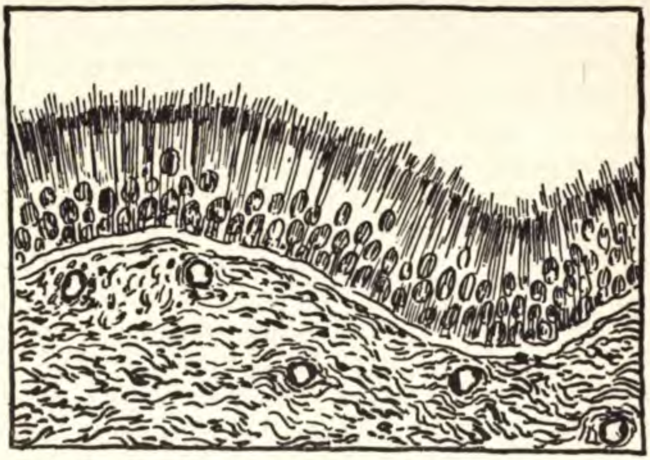

Fig. 21.—The Normal Mucosa and Substratum. The blood vessels which lie well within the firm part of the wall are small and comparatively few. (Schaefer.)

Barach[14] was unsuccessful in his attempts to demonstrate the existence of *anaphylactin* in the blood of asthmatics. A human has usually marked *eosinophilia* during a paroxysm of asthma whereas a guinea pig according to the experimental work of Herrick[15] suffers no change in the number of his eosinophiles during anaphylactic shock. Bienenfeld[16] found the blood changes in anaphylaxis to consist of a slight leucopenia, the reduction being in the polynuclear cells; there were no changes in the number of eosinophiles.

Kolipinski[17] gives the following splendid *description of* one of the common types of anaphylaxis in man: "*Hay fever* begins with a sudden excess of sneezing, with fullness of the nose and throat and an abundant discharge of watery mucus. Owing to swelling of the nasal mucous membrane, the breathing soon becomes oral. The eyes become congested, the lids swollen and red, lachrymation is increased and there is mild photophobia.

"The external nose, likewise, is swollen and red, the face puffy and the eyes less prominent. Taste and smell are impaired and from this the appetite also. From *the nasal hyperemia and infection,* the engorgement of the mucous membrane *spreads to* the accessory sinuses of the nose, to *the pharynx,* soft palate, uvula, tonsils, *and larynx,* the results being inconvenience in swallowing, tickling of the roof of the mouth, irritative uvular cough and huskiness of the voice even to aphonia. The *oppressed breathing,* nasal discharge, sneezing, and coughing, annoying enough by day, are *intensified by night* which is restless or sleepless."

Is it not rational to assume that in asthma from anaphylaxis, of which hay fever asthma is a typical example, the *swelling* and edema *and infective process* simply extends *into* the *bronchial tubes,* and that the distressed breathing, coughing and sneezing offer sufficient mechanical disturbances in the pulmonary and bronchial circulations to cause an already existing swelling to become of sufficient grade to make the exit of air difficult?

It has been my observation that *asthma supervenes* on the primary hay fever very *gradually* and usually only after several seasons of the hay fever. The patient may even be conscious that there seems to be an extension to the lower respiratory tract of the process which has existed in the upper portion.

Missildine[18] caused an *anaphylactic reaction* in a child with "horse" asthma by spraying horse serum into the nose. Immediately there came a paroxysm of sneezing, coughing, violent lachrymation, and irritation and swelling of the nasopharynx. This continued a short time and asthmatic dyspnea began. In Talbot's[19] six cases of anaphylaxis there were positive signs of *vessel turgescence* of, and increased secretion from the bronchial mucosa.

Goodale[20] has found, in a study of 340 patients exhibiting *vasomotor disturbances* in the upper respiratory passages, that such conditions can be divided into two main groups—the *seasonal,* and the perennial. In the former are hay fever and "hay" asthma in which the exciting protein is the pollen of flowering plants and comes chiefly in the fall. The latter occurs at any time in the year.

He suggests that there may be a form of the vasomotor disturbance in which the protein is bacterial. In certain individuals exhibiting the *perennial vasomotor disturbance*, an application to a scratch of the skin of soluble extracts of staphylococcus pyogenes albus, aureus and citreus, the micrococcus tetragenes, and an unidentified bacillus resembling Friedländer's bacillus causes an immediate and characteristic reaction. The reactions in any two cases may differ for each organism.

It is now fairly definitely established that the *anaphylaxis* is probably a violent *atypical inflammatory reaction.* We have known that certain disturbances, notably bacterial organisms, produce a certain more or less definite response from the tissues when brought in contact therewith. The classical signs of inflammation are given to the student as swelling, redness, heat and pain. These are about what occur in an anaphylactic reaction.

The bacteria with few exceptions have no poison but their own proteins. According to Vaughan[21] the chemistry of the protein matters not, for if any *protein* comes in contact with the tissues and is absorbed by them, it produces the inflammatory or anaphylactic reaction, provided sensitization has previously taken place. Otherwise it is *split only very slowly into its component parts.* Therefore, it is to be expected that individuals who are the victims of frequent coryzas, bronchitides, etc., will show sensitization to the *proteins* of the nose and throat bacteria and this must be a very essential element in asthma.

Since it is definitely proved that anaphylactic reactions may play a decided part in predisposing to and causing asthma, it is *important to know whether the human family, when once sensitized to a foreign protein, can be desensitized.* Besredka[22] found that serum sensitized guinea pigs could be given small doses of the serum and thus be rendered immune to otherwise fatal doses.

Schloss[23] had a child in his care that developed an anaphylactic reaction on eating or having applied to the skin, egg, oatmeal, or almonds. Administration of egg white in capsules rendered the patient immune to eggs. Talbot[19] was able *to immunize* his *cases* *of* egg *anaphylaxis* by giving small doses of egg in capsules over a considerable period of time. Others have reported that cases of hay fever have been immunized to the pollen causing the anaphylaxis by hypodermic injections of it in small doses, gradually increased. The most difficult part of the problem is the discovery of the particular protein which is responsible for the trouble. Milne[24] makes use of watery extracts of triturated pollens placed on scratches of the skin to ascertain the nature of the material responsible for the hay fever. The extract found to set up the allergic reaction is then used for therapeutic purposes. He advises that the extract be diluted so as not to produce an attack when injected. Each subsequent dose should be gradually increased and given on every third day. It has been his experience that eight to ten doses usually suffice to desensitize.

It seems to me we must conclude that *anaphylaxis* is in some cases a predisposing or *contributing factor only*, and not the common or direct etiologic factor. In many cases, however, it may be the one element without which there is no asthma.

The foreign protein when present causes circulatory change, swelling and a *lowered resistance* of the part affected. *Bacterial invasion* occurs and pharyngitis, trachitis, bronchitis, etc., soon result. *Nonpassive expiration* develops and induces the circulatory change which brings on typically asthmatic dyspnea.

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## CHAPTER XVI.

## REFLEXES, NASAL POLYPS, SINUSITIS, AND ASTHMOGENIC POINTS.

Since Voltolini[1] first reported the cure of a case of asthma by the removal of nasal polyps, there has been much speculation on the subject, and many cases have been reported in which various *pathologic conditions of* the *nose* and adjacent respiratory passages were thought to be the indirect if not the direct causes of asthma.

Not the least interesting are the so-called *asthmogenic points.* These are usually in the nose but may be in the pharynx, the trachea, or possibly the bronchi. The asthmogenic areas seem to be particularly sensitive to irritation so that merely touching a probe to them sets up coughing, sneezing, lachrymation, and mucous secretions, and may lead to an asthmatic attack in those susceptible in the same way, I hold, as may coughing and sneezing from any other cause. Those with asthmogenic points but an otherwise normal mucosa will likely not be affected so as to develop the asthmatic dyspnea.

As regards the *absorption of protein* from sinuses or other abscesses to induce an anaphylactic reaction, I can only ask the questions, "What evidence have we that absorption of the protein goes on periodically from these places, and why are there so few persons who have asthma when so many have sinus infections or other abscesses and all persons have muscle fibers in their bronchi?" The foci of infection, however, may assist materially in keeping up bronchitis either by direct extension down the respiratory tract or through the blood and lymph. A primary tuberculous focus in the lungs may make good soil of the bronchial mucosa for the many invading organisms which may have their primary locations elsewhere in the body.

I am of the opinion that the conditions in the various parts of the body which tend to *reflexly produce asthma,* do so *by* causing *coughing,* sneezing, mental or physical excitement or exertion, or some other condition which aids in bringing about an increased intraalveolar pressure or a damming of the blood into the vena cava and the bronchial veins in some other way. The cure of the local condition in the nose, pharynx, trachea, or other part of the anatomy may sufficiently reduce the tendency to a heightened intravesicular tension so that the asthma disappears.

Hänisch,[2] Schaefer,[3] Porter,[4] Daly,[5] Fränkel,[6] Hach,[7] Schmiegelow,[8] Abbott,[9] Heymann,[10] and others offered confirmatory evidence of the *importance of* giving attention to the abnormal *conditions* found *in* the *noses* of asthmatics. Bosworth[11] found nasal trouble in each of his 80 cases. Matthews[12] says of 200 cases diagnosed as asthma, 184 had significant lesions in the nose, accessory nasal sinuses, or nasopharynx; 157 of these had evident purulent discharges. Francis[13] found mucous polyps in 36, marked obstructive lesions in 27, and the nasal passages apparently free in 379 out of 442 cases of asthma. Schmiegelow[8] reported 139 cases of nasal polyps of which 31 had asthma, and 514 patients with chronic rhinitis, of whom 40 were asthmatics. Schech[14] found nasal complications in 64 per cent of his cases of asthma. Böcker[15] found nine cases of asthma among 310 persons with nasal polyps. Lublinski,[16] had 500 cases of asthma, 143 of whom had nasal abnormalities. Becker, Hertz and Schmiegelow[17] in 649 cases of nasal polyps found asthma in 47. Luce[18] thinks asthma is to a variable extent dependent upon nasal conditions. This relatively small number of statistics of those possible to obtain on the frequency of asthma and nasal abnormalities is probably somewhat misleading as the reports are in the main made by those who were thoroughly convinced that asthma is dependent upon nasal conditions.

Bosworth[11] gave each of his 80 patients surgical *treatment* and his figures indicate that 46 were cured and 26 others improved; yet he adds in another paragraph that he used also three additional remedies; namely, iodide, zinc, and belladonna. Matthews[12] treated 104 of his cases locally either with application of medicinal agents or operation, and 31 were entirely relieved of asthma, 32 markedly improved, 19 slightly improved, and 22 unimproved. Francis[13] claims to have cured 300 cases of asthma irrespective of the presence of nasal lesions by cauterizing the nasal septum. The most satisfactory place to treat, he says, is opposite the outer third of the middle turbinate. In Lublinski's[16] 143 cases, 27 were cured and 13 improved of their asthma by operation. In Schmiegelow's[8] 56 cases, 32 were cured and 11 improved by treatment of the nose. In Heymann's[10] series of 54 cases, 29 were improved and 14 unimproved by operation. Grant[19] operated 44 cases and obtained cure in 8 and improvement only in 27. Wall[20] operated 23 cases, all being cured. Abbott[9] treated 44 cases of asthma by operating upon hypertrophied middle turbinates and all but two of them were improved. Stenhouse[21] reported a case in which removal of the nasal obstruction caused the asthma to disappear, evidently cured. Luce[18] in conjunction with other treatment gave attention to the nose in 43 cases and claims much better *results* than he has seen from any other methods.

Bichaton[22] reported a case where *cauterization* of a spot on the septum relieved the asthma. Avellis[23] recommended *homes for asthmatics* where they would be under the care of rhinolaryngologists and neurologists. Latham[24] finds light cauterization of the hypersensitive area of the nasal mucosa of asthmatics very beneficial. He thinks it rarely cures, but that it reduces the irritation of the nose and the consequent reflex stimulation of the center of respiration from dusts and other irritants of the air.

Bresgen[25] advises the use of *electrolysis* by a long needle on the mucosa of the nose. Gogomann[26] reports the cure of a case of asthma by the destruction of a nasal synechia, a straightening of a nasal septum and the ablation of tonsils containing caseous accumulation. Möller[27] directs his treatment of asthma (1) to the nose by cauterization of the asthmogenic spots, and (2) to the respiratory center by suggestion.

Wassermann[28] has seen only slight results from the intranasal operations and smoking cures so commonly used. He *advises against operations* on asthmatics and directs his efforts toward tamponing the nostrils with packs carrying some anesthetic, to be left in place for fifteen minutes. He thought reflex stimuli from the nose were thus reduced. Sokolowski,[29] after various nasal operations on more than 20 cases of asthma obtained a permanent result in but one case.

While a casual reading of the reports on the beneficial results obtained in asthma by operation on the nose might indicate that this condition was a prime factor, we must hold in mind the fact that it is not the custom to publish *negative results*. The man who constantly gets negative results soon loses the enthusiasm necessary for following up the problems.

I believe that the reader will have no difficulty in understanding that it matters not where the primary focus of infection is, the respiratory passages and the breathing may be affected therefrom. The nose, when not normal, predisposes to *abnormal breathing, coughing, sneezing,* etc. Every case of asthma should have the nose inspected and treatment administered if indicated.

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# CHAPTER XVII.

## TUBERCULOSIS AND ASTHMA.

Cruvelhier,[1] Andral,[2] Bayart,[3] and Mairet[4] each described a type of *miliary tuberculosis* with a dyspnea which had all the characteristics of an acute *asthma.* Pujade[5] was of the opinion that essential asthma and tuberculosis could not be associated and hence he spoke of the dyspnea occurring in the tuberculous as *pseudo-asthma.*

Brügelmann,[6] Sarda and Vires,[7] Grasset,[8] Rancoule,[9] and Baur[10] held *asthma* to be *antagonistic to tuberculosis* and never secondary to it, but always primary. Brügelmann says that a tuberculous patient can more easily become asthmatic than an asthmatic can become tuberculous. Fränkel[11] believed that asthma and tuberculosis were rarely found in the same patient. Pannwitz and Jacob[12] in a study of 3295 patients with various diseases, found four with the combination of asthma and tuberculosis.

Landouzy[13] expresses the view that pulmonary *tuberculosis might produce* the same sort of a nervous state of the lungs as was thought sometimes resulted from the faucial tonsils. He also suggested that *asthma* might be an anaphylactic reaction to the tubercle bacilli. James[14] believed that asthma might terminate as tuberculosis. Roboule[15] spoke of pretuberculous asthma, meaning that there are individuals with a nearly inactive tuberculosis manifesting itself by producing asthma. Jessen[16] makes the statement that tuberculosis and asthma are seldom found complicating one another.

Romme[17] gave as his opinion that it is fairly well established that there is a type of *asthma* which is *dependent upon tuberculosis.* Osler[18] observed that one of the early signs of tuberculosis might be asthma with its wheezing and sibilant râles. Burgeois[19] holds that there is such a thing as tuberculous asthma.

Soca[20] studied 140 cases of asthma especially to discover the presence or absence of tuberculosis. He concludes that 120 of them were positively tuberculous. Later he reported on a series of 700 cases of *asthma* and his opinion was that *nearly all* of these were *tuberculous.* It is his conviction that nearly all cases of asthma are tuberculous.

*Reynier,*[21] in an article of considerable length on the subject of asthma and tuberculosis, drew the following *conclusions:* (1) Asthma and tuberculosis cannot be regarded as the result of the same sort of a diathesis. (2) The essential asthma of infancy presents a certain amount of immunity to tuberculosis. (3) In the event that an asthmatic becomes tuberculous, the tuberculosis develops independently of the asthma. (4) Asthma is in no manner dependent upon tuberculosis. He appends, however, that certain cases of pulmonary tuberculosis present a type of dyspnea identical with that of essential asthma.

Hoffmann[22] believes that a definite reciprocal exclusion has been assumed to exist between asthma and tuberculosis. He holds that when the *two diseases do exist in one individual* each gives up a part of its characteristics. He says the attacks of asthmatic dyspnea become weak and indistinct and the tuberculosis becomes a fibroid phthisis. Giffin[23] in a series of 82 cases of asthma, found three who were positively tuberculous. He expresses a suspicion that many of the asthmatics may have a latent tuberculosis, when he says, "The first case would seem to indicate that the possibility of the occurrence of early tuberculosis with asthma is merely a question of diagnosis." Hedenius[24] reported five cases of asthma that also had tuberculosis, but he thinks asthma and tuberculosis are not interdependent.

Frankfurter[25] reports eight cases of asthma which he had seen in the course of six years and in all he found signs of tuberculosis. On the basis of this he administered tuberculin treatment; and he claims much improvement therefrom for all. His conclusion is that *tuberculosis and asthma* doubtless have a causal *interdependence.* Turban[26] and Nalda[27] each found a small percentage of their asthmatics to be tuberculous.

The discovery of enlarged *bronchial lymph glands* in asthmatics was first reported by Chelmonski[28] who had a series of 18 cases. The enlarged glands may be accepted as evidence of pulmonary tuberculosis.

Rongel[29] investigated 101 cases of asthmatic children and found that 50 of them gave a positive von Pirquet *tuberculin test.* Krez[30] is of the opinion that most, if not all cases of asthma are tuberculous. Seventy-five per cent of his cases of asthma gave positive evidence of tuberculosis. Of the remaining 25 per cent, many gave histories that led him to suspect tuberculosis.

Tauszk[31] thinks that there is a type of asthma which is tuberculous. He makes the significant statement that very often the nature of the *tuberculosis* is such that it is very *difficult to diagnose.* Spengler[32] thinks there is a definite relationship between tuberculosis and asthma. Lawrason Brown[33] is of the opinion that cases of chronic tuberculosis not infrequently develop asthma.

Rozenfeld[34] reports that out of 40 cases of asthma he has seen in sixteen years, he thinks there were eight cases only in which tuberculosis could not be charged as being responsible for the asthma. Rozenfeld also reports that Dluski found only one case of tuberculosis and asthma in 2450 sanatorium cases; in his earlier practice he had seen two cases of asthma complicated with tuberculosis.

Galechi, according to Rozenfeld, found in 863 cases of illness, two cases of asthma with tuberculosis. Rozenfeld concludes that because of the general distribution of tuberculosis the complication of it with asthma is no more than is to be expected and that there is no reason to assume that the two are interdependent. Dünges[35] says he is led to the conclusion that many cases of asthma are tuberculous. Koessler and Moody[36] found a small number of cases in which the *tubercle bacilli* could be *demonstrated*; Berkart's[37] findings were similar.

It will be generally conceded by all that at least a large percentage of asthmatics are the victims of a chronic bronchitis. Cabot[38] has found that most diagnoses of chronic bronchitis should in reality be pulmonary tuberculosis. This leads me to say then, that a large percentage of all asthmatics are tuberculous.

The study of my series of over 50 cases brings me to the conclusion that nearly all of them were tuberculous. Only 10 per cent showed tubercle bacilli; it is not to be expected that the disease would be far enough along in most cases to show tubercle bacilli. A study of the literature reveals quite conclusively that during the last decade there has been a *reversal in the minds of many* concerning the association of asthma and tuberculosis.

It is difficult to conceive how bronchitis can be commonly maintained indefinitely, sufficiently so at least to be the cause of an asthma, unless there is either a *tuberculosis* or a *syphilis* or both of the lungs and bronchi.

In *childhood,* however, each of the infectious diseases of that period is prone to last for weeks or months and each tends to involve the respiratory passages. A second attack may follow before the other is entirely well or within a relatively short interval at best, so that a child may go for nearly a year or more without much of an interval in which he is free from respiratory tract infection. And this, theoretically at least, may happen without an involvement of tuberculosis. The consensus of opinion of the better medical men of the present day seems to be that the infectious diseases of childhood often prepare the soil, however, for the reception of the ubiquitous tubercle bacillus.

*The difficulty* lies (1) in making the diagnosis of tuberculosis, and (2) in being sure that the tuberculosis found is contributary to chronic bronchitis unless one assumes that the existence of the latter is proof of the former. The actual signs of tuberculosis in the chest of a person with only a slightly active lesion may be no more distinct than in the average individual who seems to be perfectly well.

It is the *rare adult chest in which* a careful physical and roentgen ray *examination fails to find some evidence of a tuberculous induration.* That the lesion found is tuberculous, responsible for the bronchitis, and in turn for the asthma, is probably difficult or impossible to determine for many of the cases.

But by a thorough study of case histories, careful physical examinations and a conscientious course of reasoning, I believe one will be led positively to *conclude* that many asthmatics not only have *tuberculous foci* but that these foci are very slightly active—sufficiently so to instigate and *contribute* to *chronic bronchitis.*

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# CHAPTER XVIII.

## EMPHYSEMA.

Emphysema may, in fact is nearly sure to, develop concomitantly with asthma. But it may be well to briefly rehearse the mechanics of its development. Practically all writers on *asthma* have referred to the *associated emphysema.*

*Emphysema,* like asthma, is *due to* a heightened intraalveolar *air tension.* Normally, expiration takes place passively and the intravesicular air tension even during expiration is but slightly greater than that of one atmosphere, whereas during a nonpassive expiration it increases proportionately to the force applied. The length of time the expiration endures is obviously also of importance.

The *"muffler-" and "valve-"* like construction of the bronchiole and its branches has been explained in previous chapters, and fully accounts, I believe, for the manner in which nonpassive expiration produces a heightened intraalveolar air tension.

*Nonpassive expiration,* as has been said, may be coughing, sneezing, laughing, yawning, or simply an ordinary act with force applied to it. Whether a constitutional inherent weakness of the tissues of the alveolar walls exists or not is purely problematical. It seems reasonable to suppose that there are all grades of strength or weakness—from very weak to very strong—of the tissues of the alveoli of various people, just as there are all grades of intellect from the weak to the brilliant, from the idiot to the genius.

Since the development of my ideas on this subject, and since much of the preceding chapters has been written, and during my delving into the multitude of contributions to the subject of asthma, I have come across a *chapter on emphysema* in Osler and McCrae's Modern Medicine by Dr. H. A. Hare[1] which I am glad to recognize as earlier work than mine. I was especially pleased at finding it, as it gave me further confidence in the correctness of my own channels of reasoning. I append a liberal quotation from Hare's exposition. Although the two were developed independently, my conception, as

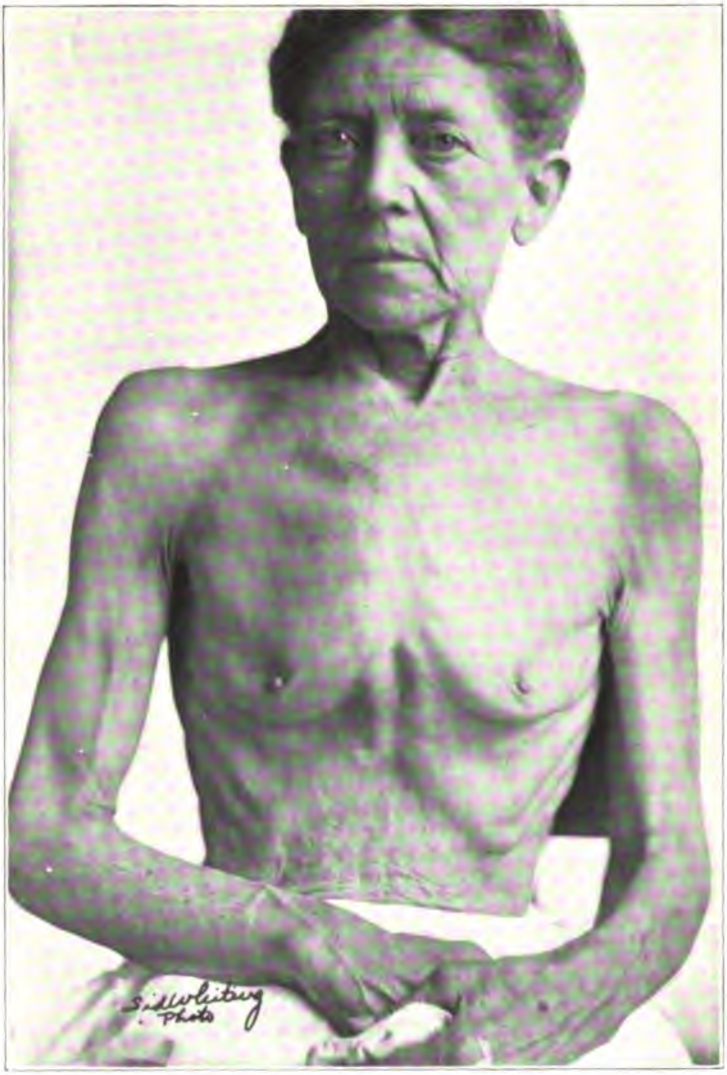
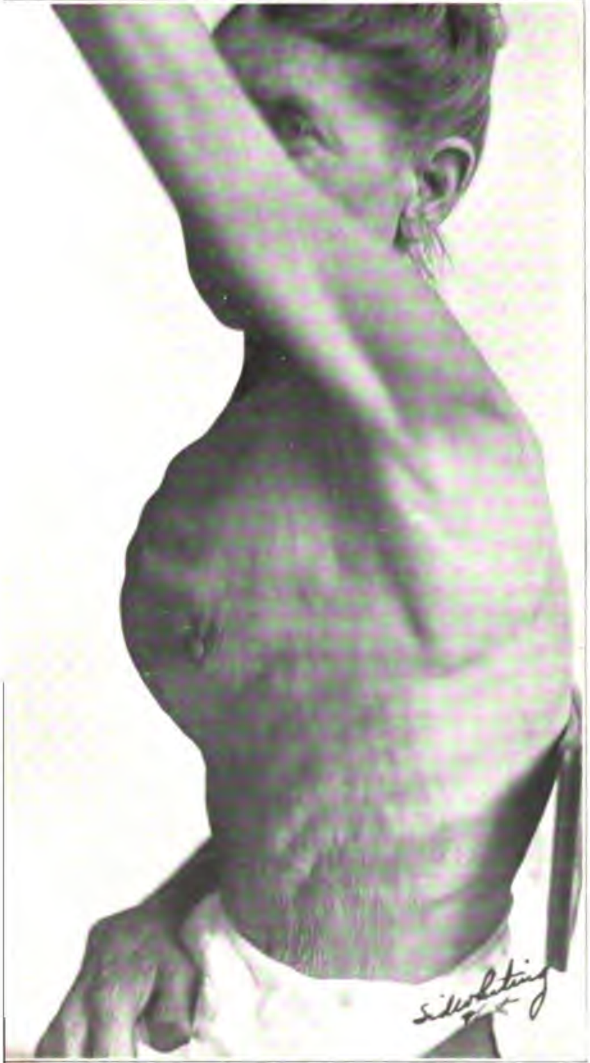


Fig. 33. Emphysemic Chest. (Front view.) With asthma, emphysema invariably de

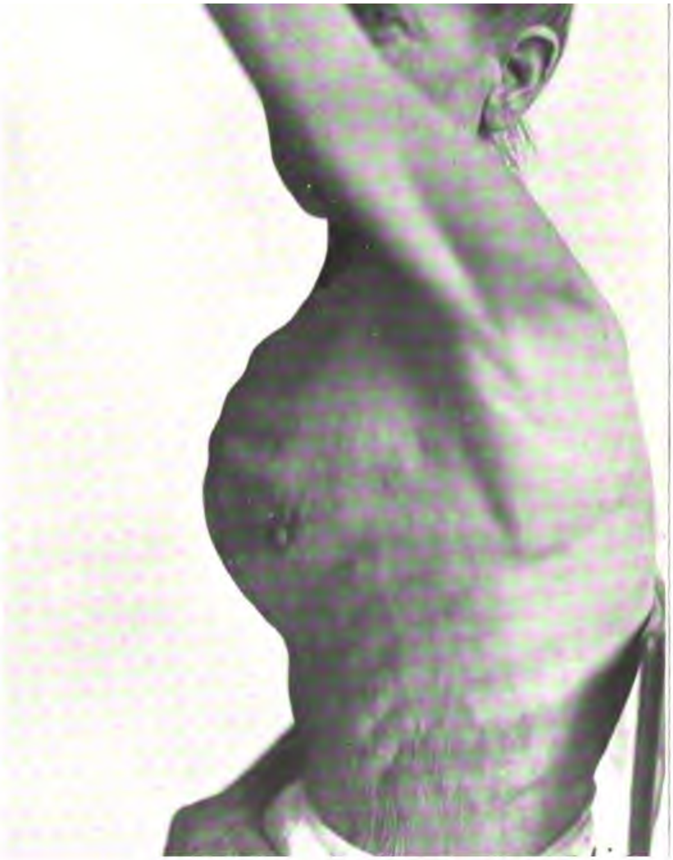


mic Chest. (Lateral view.) The sternum and anterior part of t
into the position of extreme inspiration.

"In a person suffering from advanced emphysema, inspiration is short and quick while *expiration* is much *prolonged.* A considerable influence is exerted upon the intensity of the dyspnea by the degree of severity of the associated bronchitis; thus when exacerbation of the latter occurs and the secretion in the tubes becomes more copious, the difficulty of respiration will be augmented, whereas on the other hand, during periods of comparative freedom from cough and bronchial catarrh, only slight dyspnea is experienced. There is nothing peculiar about the cough. As it is more or less constant, it not only harasses the patient, but saps his strength as well, and moreover, hastens the development of cardiac complications. The weakness of respiration, the mechanical effect of the retained air upon the lungs, the paroxysm of coughing, all serve to make aeration of the lungs defective and consequently diminish oxygenation of the blood."

Hare's assumption that the momentum of the air during coughing is cut down only at the larynx is the essential point where his theory of emphysema differs from mine. I think the contraction of the larynx in coughing simply directs the current of air toward the focus of irritation and does not materially inhibit its passage. The suggestion has been made to me by Shoemaker[2] that the localized emphysema commonly found side by side with nonemphysematous areas is proof that the *chief obstruction* is in the lobule itself.

*Trousseau,*[3] *in 1867,* looked upon emphysema as the result of nonpassive expiration as will be seen from the following: "Although *emphysema* is not a cause of asthma, it may yet be an *effect of* it and you will see how. An asthmatic individual inspires more slowly and more deeply than the man who breathes freely while instead of expiring passively as in the physiological condition, in virtue of the elastic force of the lungs alone and of the relaxation of the muscles which contracted during inspiration, he expires actively and in a more violent manner. In spite of the efforts which accompany expiration, the air is expulsed more slowly than in the normal condition on account of the obstacle to its passage produced by the spasmodic constriction of the bronchi which it traverses. It is conceivable, then, that if *asthma* has existed for a long time, pulmonary emphysema may result from



the effort at expiring, recurring at each paroxysm and being frequently also attended with cough which consists in still more expiratory efforts.''

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# CHAPTER XIX.

## PATHOLOGY OF ASTHMA.

Since asthmatics rarely die of asthma, the *postmortem findings* on the condition are *scant*. And since in the main, the changes are physiologic rather than anatomic, the latter would naturally be very slight except in a well marked chronic case. Osler,[1] Dieulafoy,[2] and von Strümpell[3] in their texts say nothing of the pathologic anatomy of asthma. Anders[4] says, "The morbid changes peculiar to chronic bronchitis, pulmonary emphysema, and right ventricular hypertrophy with dilatation are found at autopsy."

I find in the last edition of Berkart[5] and in an article by Ellis[6] the *collected records* of autopsy findings in seven and eight cases respectively of asthma, being, they say, all that the literature of the last twenty-five years contains. To this number I add the ninth.

*Case 1,* reported by von Leyden,[7] female, 40, was subject since infancy to typical attacks of asthma. She was addicted to morphin and in late years of life dropsy and albuminuria developed as serious complications. The physical findings and the character of the sputum were typical of asthma. She died in an asthmatic attack.

The postmortem examination showed extensive vesicular emphysema, large bullæ showing in places, lungs pale, bronchial mucous membrane red, and within the lumen of the bronchi were mucus and a greenish white detritus. Microscopic examination showed many dilated alveoli; walls of bronchi were somewhat altered, containing on the free surface a sticky substance.

*Case 2,* reported by Berkart,[5] female, 37, for fourteen years had had asthma, and death came in a paroxysm of that affection. The autopsy record is hypertrophied and dilated right and left ventricles, lungs dark in color and emphysematous, the mucous membrane of the bronchi was dark, the capillaries were injected and dilated, and the surface of the walls contained layers of mucus. The walls of the bronchi were thickened and there was hyperplasia of the mucous membrane. The bronchioles were dilated.

*Case 3,* reported by Schmidt,[8] female, 49, had suffered but little over six weeks with asthma during an attack of which she died. The autopsy findings were, heart large, right ventricle dilated, emphysema, smaller bronchi dilated and filled with a homogeneous mass, embedded in which were desquamated alveolar epithelium.

*Case 4,* reported by Fränkel,[9] male, 63, had had asthma for three years and death resulted from an asthmatic attack. The autopsy revealed moderate dilatation of both ventricles, the lungs markedly emphysematous with bullæ the size of cherry stones; the bronchi were somewhat dilated and partially filled with threads of mucus. The walls of the bronchi were thickened and the mucous membrane intensely congested with areas of cicatricial tissue. In the smaller bronchi the epithelium was much denuded.

*Case 5,* reported by the same author, male, 48, was asthmatic for many years during the latter part of which occurred almost daily attacks. Death was from cardiac weakness. The bronchi were dilated and filled with spirals and the mucous membrane was hyperemic, with here and there extravasation of blood.

*Case 6,* reported by von Jezierski,[10] male, 62, suffered for five years from asthma and died from lobar pneumonia. The autopsy showed marked emphysema, the bronchi were dilated, mucous membrane was red and in places there were dendritic fibrinous coagula, and mucus with epithelial cells, leucocytes, erythrocytes, and eosinophiles. The bronchial walls were thickened by a new formation of vascular elastic tissue.

*Case 7,* reported by the same author, female, 46, had for twelve years suffered from asthma and died during an attack. The autopsy revealed emphysema, bronchioles dilated and partially filled with stringy mucus, and the walls of the bronchi showed infiltration with small round cells.

*Case 8,* reported by Ellis,[6] male, 27, died of heart failure following a very severe and prolonged attack of bronchial asthma. The dyspnea was of the expiratory type and had existed for at least a year. The findings revealed hypertrophy of the left heart, dilatation of the right ventricle, pulmonary emphysema, purulent bronchitis and an exudative bronchiolitis and many plugs and clots in the bronchi.

The diameters of the smaller bronchi were 0.13 to 0.16 mm., and the bronchi were partly filled with detritus consisting of mucus and a few embedded cells, for the most part degenerated epithelium. In some of these bronchi the mucus was in spiral forms. The cells of the walls were rarely detached.

In the larger bronchi were more pus cells and desquamated epithelium. Some of the endothelial cells in the tubes 0.8 mm. in diameter were very much elongated. The walls were markedly infiltrated with leucocytes, usually polynuclear in type. Eosinophiles were also found occasionally both in the walls and the lumen, being very numerous in the larger tubes. Occasional hemorrhagic areas were found in the bronchial walls. Hyaline degeneration existed in the walls of the larger bronchi down to the basement membranes and in the tunica propria. There appeared to be no changes in the muscle or the elastic coat. The alveoli were distended and the walls often ruptured.

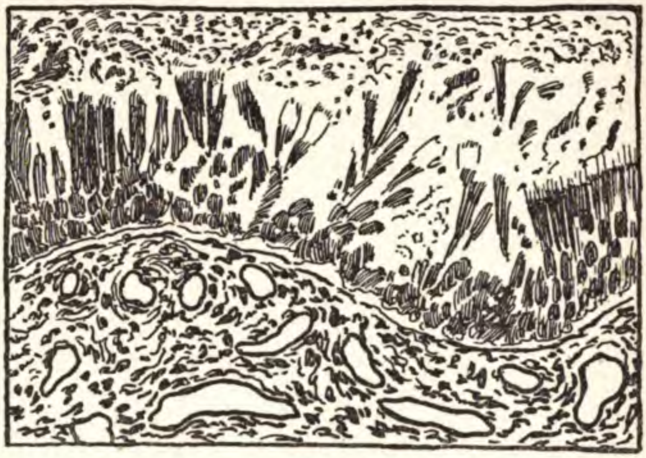

Fig. 24.—The Mucosa and Substratum in Chronic Bronchitis. In chronic bronchitis the blood vessels of the stratum just beneath the mucosa become very much dilated. It must be remembered that the dilatation which can be demonstrated by the ordinary histological methods is that which remains after the normal elasticity of the tissue has acted, and after the fixing fluids have had their contracting effects. That severe grade of dilatation which comes only in the paroxysms of asthma cannot be demonstrated microscopically. But even with the demonstrable grade of dilatation plus the dilatation of the minute capillaries, not histological ordinarily, one can easily see how the swelling of the mucosa thereby produced during expiration could be of such a grade as to seriously hinder the exit of air. (Delafield and Prudden.)

The following case I report from my St. Louis City Hospital service. The autopsy was performed by Dr. E. N. Tobey.

*Case 9,* male, 56, had suffered with typical attacks of asthmatic dyspnea for eight or ten years. During the two or three months preceding his death he developed a myocardial inefficiency with signs of a mixed cirrhosis of the liver. Death resulted from pneumonia. For the last two or three months of his life he had no asthma.

Autopsy findings were as follows: well developed white male, 167 cm. long and weight about 186 pounds. The *body* has a slight yellowish tinge, some edema of the lower extremities, no lividity and no rigor mortis. The body heat is still present. The conjunctivæ are yellowish; the right pupil is slightly larger than the left. The subcutaneous fat over the chest measures 20 mm. and that over the abdomen 50 mm.

On section of the thorax, the lungs are found distended, practically meeting in the midline. The pericardial sac contains about 40 c.c. of a clear straw colored fluid and on the anterior wall of the heart are several small white plaques, the largest measuring 4.0 to 4.5 cm. The *heart* weighs 540 gm. and measures 11.5 by 4.5 cm. The chamber of the right heart is considerably larger than that of the left, though both are dilated. The wall of the right ventricle measures 9.0 mm. in thickness while that of the left is 1.5 cm. The mitral valve flaps are somewhat thickened. There are a few slightly elevated yellowish sclerotic patches in the aorta, one of which is calcified. The heart contains clots though the blood is fluid.

The pleura on the right is thickened and generally adherent, and the lung is torn in removal. There is some dark brown fluid in the upper part of the cavity. The right *lung* weighs 780 gm., in places is dark reddish in color and necrotic in small areas. Because of the fluid above and the pneumonia below, there is but little air in the right lung except in the outer portions. The left lung weighs 500 gm. The pleura is thickened and adherent. The tissue is grayish, air-containing and emphysemic. The bronchi show evidences of chronic bronchitis.

In the *abdomen* there is a small amount of fluid. The peritoneum is jaundiced, the liver extends to the umbilicus and the omentum is adherent to the anterior wall of the abdomen. The liver weighs 1600 gm., is of a yellowish slate color with a hard nodular surface and a sharp edge. There is no noticeable increase in resistance on cutting. The parenchyma has a nutmeg bile stained appearance. The measurements of the liver are 27 by 17 by 8.0 cm. The gall-bladder is empty and the ducts are patent. The spleen weighs 180 gm. and measures 13 by 11 by 3.5 cm. It is dark purple in color and is congested. The pancreas weighs 125 gm. and measures 25 by 4.0 by 3.0 cm. The right kidney weighs 220 gm. and measures 14.5 by 8.0 by 3.0 cm. The cortex is 8.0 mm. and the medulla is 2.0 cm. The left kidney weighs 240 gm. and measures 13 by 7.0 by 3.5 cm. The cortex is 1.0 cm. and the medulla is 2.2 cm. Both capsules strip easily, leaving smooth surfaces. The stomach lining is somewhat injected. No changes are found in the intestines. The appendix measures 6.0 cm.

From the *standpoint of* the *asthma,* I would call attention to the hypertrophy and dilatation of the right heart, the emphysema, the pleurisy, and the chronic bronchitis, all of which indicate the chronicity of the pulmonary infections and the probability of many "colds," bronchitis, tuberculous coughs, etc.

The *sputum* of asthmatics has certain peculiarities which exist with more or less uniformity. In the early stage of the attack the sputum may be scanty or absent. Usually it will be scanty and watery in the very beginning, or possibly purulent and abundant and may change so that at the height of the attack there is a copious mucous discharge.

Curschmann's *spirals,* Charcot-Leyden *crystals,* eosinophile *cells,* other leucocytes, lymphocytes, etc., may be in the sputum. The sputum in the latter stage of the attack is generally extremely tenacious and some of it may come away as small compact masses or as fibrinous *casts* of a considerable portion of the bronchial tree.

Berkart[5] who holds that these masses when lodged in the bronchi afford the essential cause of the asthmatic dyspnea has made an exhaustive study of them. His book displays a very instructive series of drawings of *spirals and casts.* He says, "Without previous preparation some appear as straight, bent spiral threads of a gray or yellowish color varying in length and in thickness from that of a hair to that of a woolen fiber. Others look like small gelatinous and transparent bodies, resembling grains of boiled sago; still others appear as large opaque, grayish white and irregular masses. On washing them, however, in a physiological salt solution, their coating of mucus is removed and their proper shapes then become discernible. Some of them are solid, straight, nobby cylinders more than three inches in length and an eighth inch in thickness; others, thicker and shorter, have a dichotomous division; others again of greater thickness are so entangled as to resist all efforts to unfold them, while still others are spiral, nearly two inches in length.

"On *microscopic examination* the solid cylinders are seen to consist, when fresh, of round cells closely packed together between a delicate network of fibers, which, however, soon disintegrate and disappear. They generally enclose, especially in their peripheral portions, a number of cylindrical epithelial cells. They carry, moreover, on their surface as well as within their substance, sets of straight, bent or curly threads of a milk white color, strongly reflecting light, from 0.003 inch to one inch in length and corresponding in thickness. The texture of those threads, the so-called Curschmann's spiral, consists of strands each of which is formed of fibers wound round a central, white, homogeneous-looking filament and contains in its outer meshes heaps of eosinophiles and other leucocytes as well as epithelium."

Berkart says that these spirals are most readily found in sputa which have stood for some time as they are more resistant to decomposition than the rest of the sputum. Some of the spirals may be seen with the unaided eye but many only with the microscope. Riehl[11] described *spirals of unusual size;* they were 15 cm. long and had a central fiber. The small masses should, according to Berkart, be placed under a cover slip and gently flattened out. Some are hyaline casts of the alveoli and ducts, and are studded with bacteria at the margins. Casts may be found to be composed of epithelial cells.

Berkart writes, "The viscid medium in which all these solid particles are suspended contains a large quantity of eosinophilous *leucocytes,* mast and hemosiderin cells, Charcot-Leyden crystals in varying numbers and sizes, and several kinds of *microorganisms.*" He is of the opinion that the streptococcus is the organism commonly found in the bronchial discharges.

Carmalt-Jones[12] reported the finding of an asthmatic sputum with an almost pure strain of a diphtheroid bacillus. Grünbaum[13] found the chief *organisms* to be the pneumococcus and the bacillus catarrhalis. Lenhartz[14] discovered a diphtheroid bacillus and Müller[15] a pneumococcus.

Koessler and Moody[16] made perhaps the most extensive study on record of the *bacterial flora* of the sputum of asthmatics. In 28 cases they found besides the common aerobic organisms, the pneumococcus, streptococcus, influenza bacillus, and micrococcus catarrhalis, and certain anaerobic bacteria which they class under three heads, to-wit: "(1) A gram-negative fusiform-like bacillus which produces a putrefactive odor in the culture; (2) a gram-negative very small bacillus which produces characteristic black colonies on the blood agar; and (3) a very small streptococcus. These three organisms live in a certain form of symbiosis and are in every case present in the anaerobic tube."

These authors also state that they find a certain form of "asthma bronchitis" due to the *tubercle bacillus* and which can only be demonstrated by guinea pig inoculation. Berkart found tubercle bacilli in five cases. Others report similar findings.

Pirie[17] studied the *bacteriology of 15 cases* of asthma. He found the pneumococcus in 15; mucus catarrhalis group in 14; staphylococcus in 8; streptococcus in 6; Friedländer group in 6; diphtheroid in 3; mucus paratetragenes in one; influenza bacillus in one; and an unidentified organism in one.

The *leucocytes* found in the sputum for the most part are eosinophiles. Lord[18] says that both mononuclear and polynuclear types are found, but that the former are the more numerous and are mostly in and about the spirals. Aronson and Philip[19] found that 66 per cent of the cells in the sputum and 15 to 17 per cent of the leucocytes in the blood of a nine year old girl were eosinophiles, many of those in the sputum being mononuclear.

Gollasch,[20] Müller,[21] and Fink[22] each demonstrated that the *eosinophiles* found in the sputum of asthmatics were identical with those of the blood. In Fink's case, they varied from 80 to 90 per cent of all the cells in the sputum. Lewy[23] thinks that the presence of the eosinophiles in the sputum is not specific for asthma. Weiss[24] found eosinophiles in the sputum of pulmonary tuberculosis and of chronic bronchitis. Von Strümpell[25] is of the

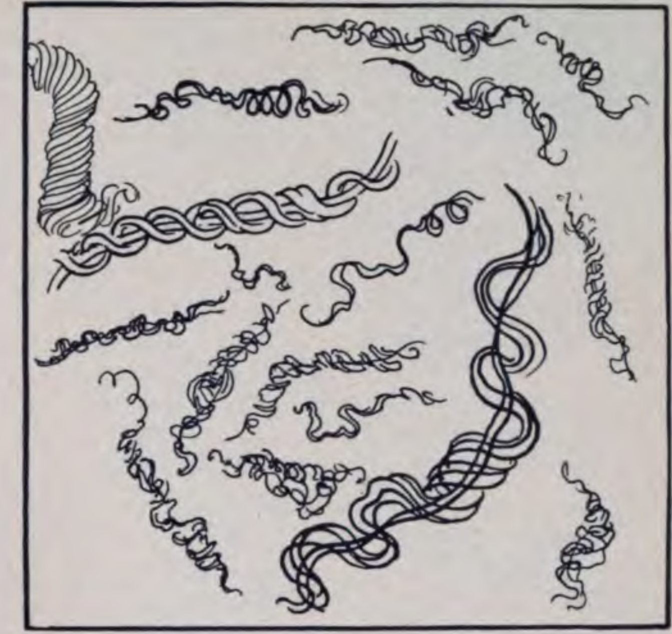

Fig. 25.—Curschmann's Spirals. In chronic bronchitis, the cilia within the bronchi whip the mucus and other inflammatory detritus into various shaped masses. Some are large enough to be seen with the naked eye but many require magnification to be seen. They commonly exist in asthmatic sputum.

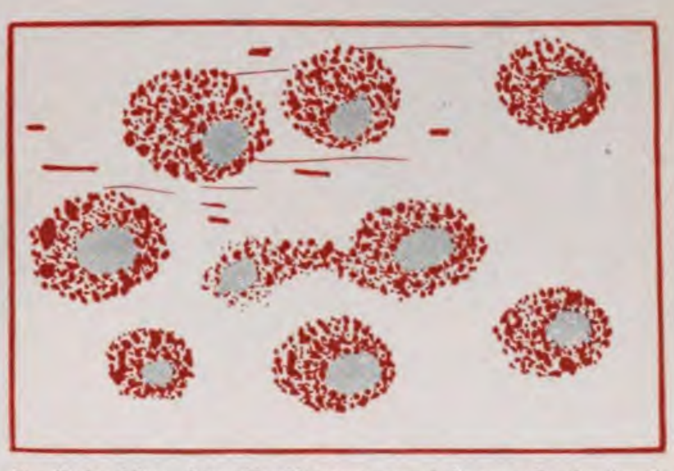

Fig. 26.—Eosinophiles. A considerable percentage of the pus cells of asthmatic sputum are eosinophiles. This is probably indicative of chronic intoxication.

opinion that the eosinophiles may exist in the sputum from a chronic catarrh of the bronchi even in the absence of asthma.

Ellis[6] holds that Kaufmann's view of the *formation of spirals* is perhaps the last word as yet. Quoting from Ellis, "He states that for the production of spirals, which consist of mucus, there is requisite the presence in the bronchi of a scanty, tough, mucous secretion which, by violent respiratory efforts, by the associated pressure and the convulsive movements, possibly also by contraction of the bronchi themselves, is formed and turned and driven forward. In this process the central part of the mucous string becomes so dense that it appears as a shiny homogeneous thread which, however, is no peculiar structure in itself surrounded by the looser spiral mucous mantel."

Predtetschensky[26] says the spirals consist chiefly of eosinophiles and mucus about a central core of mucin fibers. He holds that the *spirals,* as such, are *not pathognomonic* of asthma but of a bronchial secretion. Kaufmann[27] found spirals in bronchopneumonia, croupous pneumonia, fibrinous bronchitis and bronchial stenosis without asthma having existed in any of the cases. Ellis[6] holds that all the elements which ordinarily exist in asthmatic sputum have been found in diseases other than bronchial asthma. Vierordt,[28] von Jaksch,[29] Pel,[30] Patella,[31] Curschmann,[32] and Predtetschensky[26] each reported finding the spirals in pneumonia.

The *crystals* bearing the name of Charcot-Leyden are other elements which have been commonly found in the sputum of asthmatics and have received a considerable amount of study. They were first described by von Leyden[33] and he held them to be octahedral, and the essential cause of asthma. Charcot and Vulpian[34] also believed them to be octahedral. Cohn[35] made a careful study of them and came to the conclusion that they are hexagonal rather than octahedral, delicately elongated, double pointed pyramids, and that they are colorless, of a dull luster, and range in size from .175 mm. long and .04 mm. wide with an apical angle of 18 to 20 degrees down to so small a size that the highest magnification is required to see them.

Von Leyden[33] found them in six of seven, and Curschmann[32] in 34 of 38 cases of asthma. In the four they were constantly absent. Unger[36] was able to obtain a *deposition of the crystals by preserving sputum* in a moist chamber for a time. This led to the assumption that they likely may result as a decomposition product.

Lord[18] believes too, that it may be necessary to let the sputum stand in order to demonstrate the *crystals.* Their presence in a smear, he says, may be indicated by a *gritty resistance* between the cover glass and the slide. He holds that they are not present during the intervals between the attacks.

The *crystals* have been repeatedly *found elsewhere* than in asthma sputum. They have been found in tuberculosis sputum by Meissen,[37] in pus from emphysema by Eichorst,[38] in sputum of ordinary bronchitis by Bizzozero,[39] in the feces of patients with helminthiasis by Baumler[40] and Leichtenstern,[41] in a nasal polyp, and also in cancer of the cervix of the uterus by Lewy,[23] in bone marrow by Neumann,[42] in blood and tissues of leukemic patients by Charcot and Robin,[43] Charcot and Vulpian,[34] Eberth,[44] Lauenstein,[45] Zenker,[46] Prus,[47] and Westphal.[48] Pfuhl[49] examined the sputa of 856 cases of pulmonary diseases not complicated with asthma and found the crystals in but one case. In this sputum they were present, however, in large numbers.

Schmidt[50] reports three cases of asthma with marked acetonuria. Edelmann and Karpel[51] found in four cases of asthma that there was present at the time of the paroxysms, a cloudiness of the *urine,* due to the presence of leucocytes. Thirty per cent of them were eosinophiles. In one case with this percentage of eosinophiles in the urine, the blood contained 87.5 per cent.

A *summing up* of the pathologic findings in asthma shows (1) that the bronchi give evidence of chronic inflammation in nearly all, if not all cases; (2) that there is also evidence of an accumulation of fibrinous plugs and casts obstructing the tubes; (3) that there is emphysema; (4) that in those cases where an autopsy was performed and where notice was made of it, the right heart displayed hypertrophy and dilatation; and (5) that the bronchial muscle has not been found hypertrophied.

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## CHAPTER XX.

## THE CLINICAL HISTORY, PHYSICAL SIGNS, AND SYMPTOMS OF ASTHMA.

Any individual who has in mind a certain explanation for a given pathological condition is very likely to see those symptoms and phenomena which give the strongest support to his ideas, and he may unconsciously ignore factors not readily brought into line with his conception. In other words, a man sees in his range of vision just those things he knows are there. In order that *my prejudice* shall be neutralized, I shall, after giving my observations, take freely from the work of others, quoting their exact language where possible.

Asthma is no respecter of *age, sex* or *color*. It may develop in early life or not until advanced years. An individual may have only one, two or three attacks, but more likely when once developed it will recur at intervals usually in the seasons of the year when the climatic conditions are most changeable and trying.

Not infrequently there seems to be a *hereditary* influence, as some cases are found where asthma began in very early life and where one or both parents and perhaps one or more of the grandparents had been asthmatics. The *locality* is a factor of apparently decided moment in one case and of no influence in another. Cases occur in country and in city, in temperate and torrid zone, and in both low and high altitudes.

*Change of seasons* affect asthmatics differently, one case being worse only in winter while another is worse in summer. As regards *food, drink, habits,* etc., there seems to be no definite conclusion to be drawn—at least in favor of any positive effects other than temporary and indirect, and these likely only in isolated cases. Some asthmatics are thin while others are obese. *Asthmatics* as a rule are *neurotics,* but it should be added, so are most other individuals who have been ill and suffered much for years.

Most if not all asthmatics are subject to *inflammatory conditions* of the respiratory passages, the so-called "colds" being a frequent occurrence and these usually involve the bronchi to greater or less extent. Then too—and this I consider one of the very important points—the inflammatory condition endures usually for weeks, months, and even for years, in many of these cases, before there is even any sign of asthma.

In this connection it should be remarked that coughs, "colds," grip and *catarrhal conditions* of the respiratory tree are such *common* afflictions with so great a number of the population of the globe that the lay public particularly, and physicians too often—to a less degree, of course—are prone to regard these afflictions as unavoidable necessities and occurrences that need receive but slight attention unless complicated with pneumonia, tuberculosis, asthma, etc.

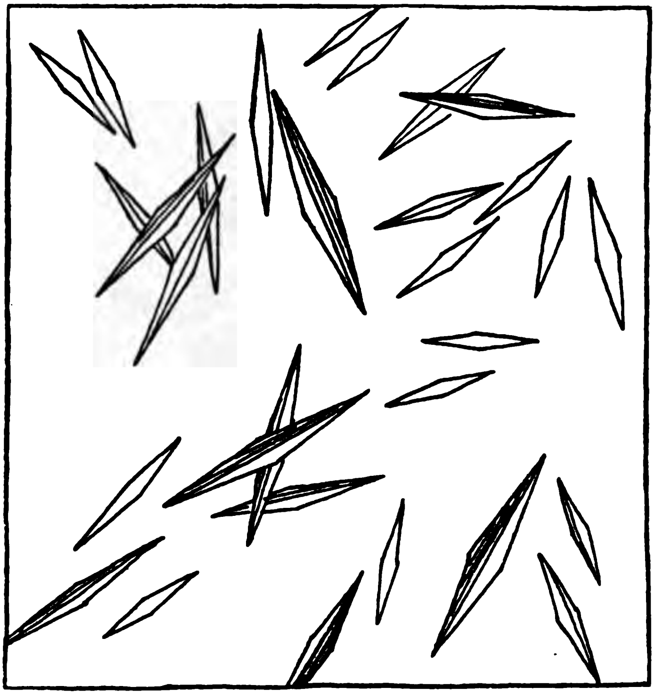


Fig. 27.—Charcot-Leyden Crystals. These crystals are formed in sputum of chronic bronchitis, especially if asthma exists. They have been repeatedly found in other locations. They seem to indicate decomposition.

I am ever mindful of a remark made by one of my internes some years ago. He said, "There is nothing interesting in our ward, nothing at all. I just cannot get my interest aroused in anything but pneumonia, typhoid, an acute rheumatic, an active heart disease or such." And is it not a fact that physicians, as a class, as well as the laity, give little heed to *minor* every day *ills?*

In this way the previous history of frequent often protracted coughs and "colds" may escape even being asked about. In no other way can I explain the facts as I see them, that the importance of *coughs* and *"colds"* as precursors of asthma has been generally *overlooked* or at least not mentioned except as an incident.

While surgery has been advancing by leaps and bounds and has been the popular field, not only for the man who desires to specialize, but for the general practitioner as well, internal medicine has received the devotion of a relatively small number of specialists and only the enforced attention of many of the general practitioners. Naturally most men do those things that are most urgent and likewise enjoy seeing immediate results of their labors. Therefore the practitioner of medicine has given freely of his time and thoughts to the acute diseases and been, if not neglectful, certainly not deeply interested in *chronic illnesses* which do not tend to endanger life.

The greater percentage of *asthmatics* have coughed vigorously and more or less incessantly for weeks, if not for months before the development of the asthma. The surprising thing in getting their histories is that many of these cases will *ignore* entirely the previous *coughs and "colds"* unless specifically asked about them. This is probably explained by the fact just given, that people pay little heed to coughs and "colds" unless complicated, and then it is the complication which receives the attention. In some histories there are evidences of the patients' having undergone heavy physical strains which may be held partially responsible for the asthma.

Some asthmatics have *hay fever,* or better, some individuals with hay fever develop asthma. The hay fever subjects sneeze and cough excessively and they also have in the upper respiratory passages inflammatory conditions which are prone to extend to the bronchi. The attacks last ordinarily six weeks or thereabouts and recur yearly. The coughing and sneezing throw a strain on the heart, large veins, and bronchial veins so that if a bronchitis also exists the bronchial mucosa has a dual reason for swelling.

The asthmatic *attacks* may come any time, day or night, but they perhaps more commonly occur *at night* and usually some hours after the subject has been asleep. Patients frequently say they awakened with an attack of difficult breathing. Then too, when inquiry is made, they will admit often that they awakened coughing and that the attack of asthma came following the coughing. Sometimes, however, the paroxysm comes on with little or no coughing, in which event it is due to position and nonpassive expiration. During the period of repose the mucus collects in the trachea and reaching the upper part, stimulates coughing; and labored breathing is thereby induced. This comes even while the patient is asleep, and, coupled with the effect of position, causes an attack to be well developed before he is awake. Or the patient awakes with a sensation of choking, and frightened by the memory of similar previous attacks, starts labored breathing and an asthmatic attack soon follows.

The *duration of* the *attack* may be for an hour or two or even less, or it may drag on for hours or even days. The dyspnea usually begins gradually with the difficulty in respiration showing at first perhaps, just as much in inspiration as in expiration. Usually in the beginning the normal relation of the inspiratory and expiratory phase is maintained, but sooner or later the expiration becomes extraordinarily difficult and relatively prolonged and the rate of respiration generally increased. The patient may or may not have observed these changes in his breathing. More or less cyanosis may develop, the respiration become audible and he is apparently suffering extreme agony.

He usually finds greatest *relief from sitting* with the shoulders and head inclined well forward and with his elbows on his knees. Or if he is standing he is apt to get some relief by fixing the arms, holding with the hands to the back of a chair or other object the better to bring more muscles into play. Ordinarily the coughing spell has begun gradually some time previous to the spasm of asthma and increased in intensity and frequency until the attack is definitely developed and even yet the cough may continue with greater or less severity.

After a time the cough begins to produce frothy liquid and later may bring up some small plugs and much viscid tenacious mucus, often very difficult to free from the lips. The *expec-*

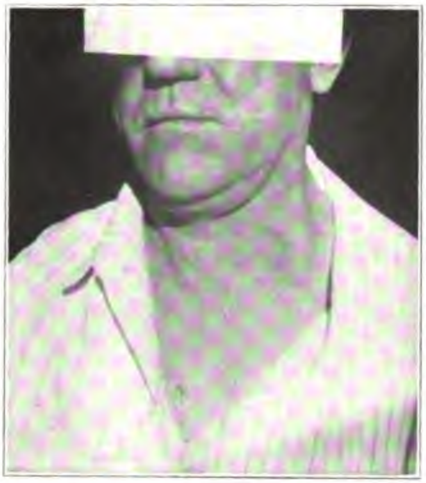
*toration* of the mucus may give some relief. This may come because the getting rid of the viscid sticky sputum actually gives more breathing space; or because the removal of the sputum relieves the irritation that has compelled the coughing and the abnormal breathing, or because getting rid of the sputum removes the cause of the fright and fear of choking. Most likely all three of these factors play a part.

Before this time has elapsed, however, the patient has usually been given one or more drugs. Generally asthma victims have suffered so severely and for so long that they have become acquainted with some few of the many much vaunted *proprietary* asthma *cures* that are ever advertised for sale. These usually contain ingredients which help to relieve the condition; and then the effort to inspire smoke or vapor or any drug will increase the time and depth of inspiration and make expiration slow and more nearly passive, thus certainly improving the condition.

On *physical examination* it will be found that some of the patients are of good physique; others are of the long slender chest, narrow costal angle, etc., of the tuberculous. Most asthmatics have arteriosclerosis or capillary sclerosis in advance of their years. I have in mind particularly close observation of the blood vessels as suggested by Graves.[1] He teaches that for the palpation of the artery, for example the radial, one should use the end of the finger so as to compress the artery between the finger and the bony background of the wrist. The pressure forces the blood out of that segment of the vessel and by moving the finger tip back and forth the artery wall is rolled and the grade of thickness may be estimated. The finger nail may sometimes be used to advantage.

The radial artery may not show thickening while other arteries may. *Capillary thickening* may be revealed by pallor out of proportion to the anemia, by dilated venules of the skin or of the conjunctiva as shown by Luedde,[2] and by a tendency to small yellowish green hemorrhagic spots from slight bruises.

These signs of slight bruises have impressed me as being of considerable significance; and I have found no reference to them in the literature. Some persons develop the spots without knowledge of having received an injury; or very slight blows leaving no signs of a bruise in some may produce large hemorrhagic areas in others.



d Neck Veins. Coughing, sneezing, and dyspnea produce heightened
ension, and this in turn hinders the flow of blood through the pulmonary
amming effect of the increased pressure is shown plainly in the jugular
apillaries, blood vessels, and lymph channels of the bronchial mucosa
iration.

The spots are ordinarily about the size of a dime, light yellowish green in color, and situated most commonly upon the legs.

The explanation which I have advanced for them has been that the capillaries in those subject to such bruises are less able to stand a strain, and hence are more easily ruptured than normally, and an extravasation of a small amount of blood occurs. Possibly there is not an actual rupture of the capillary wall; there may be just a chemical change in the wall from the injury so that diapedesis of erythrocytes takes place abnormally easily. Or again, possibly the corpuscles within the capillary are injured and it is only the hemoglobin which escapes into the tissues.

It has seemed to me that those who are subject to these spots are more susceptible to chronic and perhaps to acute disease, for I have found these spots in most cases of gastric and duodenal ulcer that I have seen in recent years. That a blow upon the abdominal wall can so injure the stomach mucosa as to permit of an action thereon by the digestive juices is a possibility; that this blow produces a sufficient injury to a spot of stomach mucosa to lower the resistance of that spot so that bacteria in the blood stream might lodge and grow there and thus allow the digestive juices to have an effect, thus producing an ulcer is a stronger possibility. In most instances, however, the changes in the walls of the capillaries are such as to inhibit the filtration and osmosis of nutritive material from the blood stream to the cells, thus lowering their resistance and making them more fertile soil for bacteria.

During spells of coughing the veins of the neck will be seen greatly dilated and the face will be red and puffed.

In cases of long standing, the chest is usually barrel-shaped and the *lungs emphysematous,* and there is apt to be evidence of a mildly labored breathing even in the intervals between attacks, especially after exercise. The heart area is difficult to outline and the heart sounds may be feeble and distant.

The *onset* of the attacks as I have seen them, comes gradually, beginning commonly after a patient has been sleeping, exercising somewhat strenuously, or restraining his cough as long as possible. When he awakes or when he ceases relatively heavy exercise he usually begins to cough. An attack, it seems, may develop from congestion of blood in the larger veins and tributaries from the horizontal position. The bronchial capillaries may be so distended while the patient is asleep in a horizontal position that he awakens with an asthmatic attack fairly well started. Even before he is fully conscious, the irritation in the bronchi from the congestion and the secretion sets up some coughing and other nonpassive expiration which is greatly increased as soon as he is entirely awake. But any nonpassive breathing may cause the paroxysm to begin. Pohlman[3] has suggested that the early morning attacks may be accounted for on the assumption that the upper trachea only is especially sensitive to the presence of mucus and that it takes usually two to eight hours for the cilia to raise the sputum to this point.

The *cough increases* in violence and the breathing becomes labored, both inspiration and expiration being affected. As the cough continues, the patient becomes anxious, the breathing growing constantly more labored. Shortly the expiration becomes very difficult and the inspiration less so. I have on several occasions seen this change of the breathing from a decided difficulty of both phases to a fairly easy inspiration and prolonged labored expiration take place almost instantaneously.

*Auscultation* reveals wheezing, sibilant and sonorous râles about the chest, especially over the larger bronchi. The sounds are those that must come from tubes not less than perhaps 2 to 3 mm. in diameter. Certainly they are not those coming from the very finest tubes. They may be more pronounced on expiration than on inspiration. In a patient who is suffering but little and who has comparatively few râles, a few hard coughs may produce a decided increase in the sounds of expiration. I have repeatedly demonstrated this point. Or a patient may be asked to breathe forcefully, especially applying muscular effort to expiration and the wheezing rapidly increases, particularly during expiration. Exercise will also tend to do this. If a patient in the asthmatic state, but comparatively free from an attack, is sent up two or three flights of stairs, a paroxysm may be induced. At any rate the sounds of the chest will be increased over what they were. Not infrequently will it be reported that an attack is induced by exercise, particularly if unusual in character.

The *blood pressure* during an attack I have found to be somewhat increased. This I think is due to the tonic contractions of the skeletal muscles of the body during the paroxysm, plus the

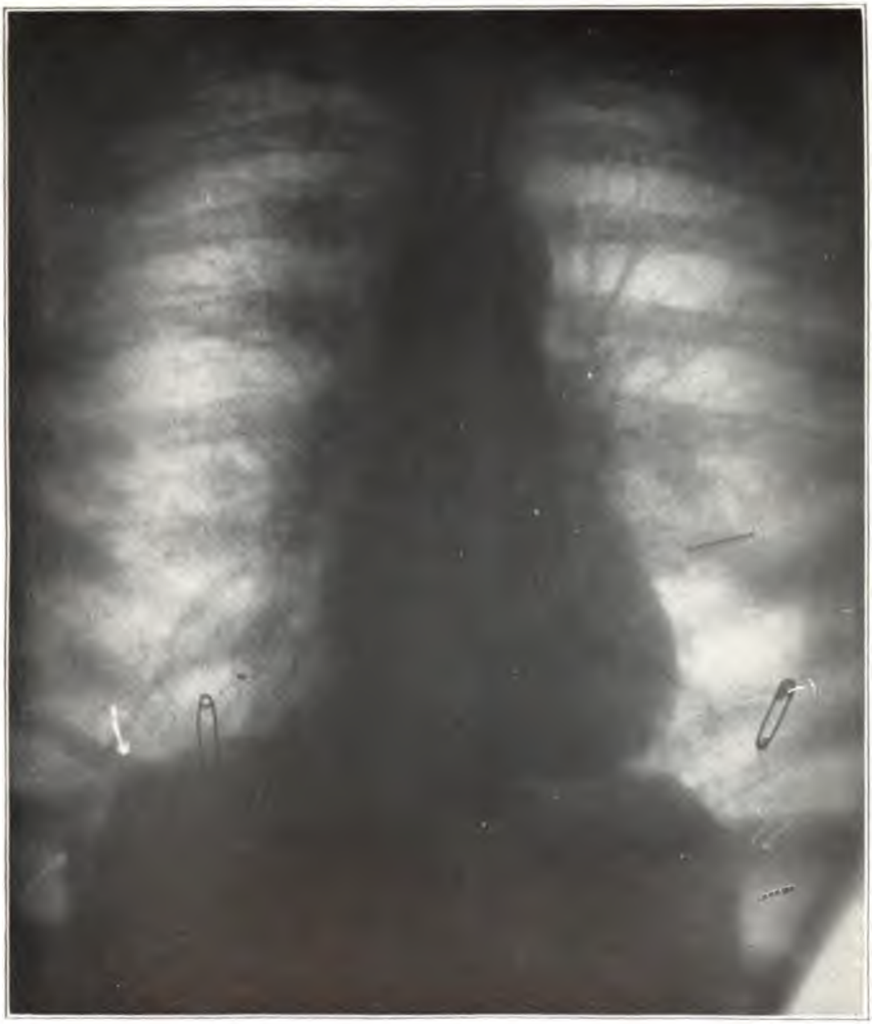


Fig. 29.—Roentgenogram of Case 17 in Chapter XX. Attention is called to the following: the thickened prominent bronchi, indicating chronic bronchitis; the small tent-like bulgings of the diaphragm indicating pleural adhesions, likely tuberculous; the nearly horizontal position of the ribs; the relatively high and prominent aorta; and the shadows in various parts of the lungs, notably throughout the right lung and about both hila.

marked forcing of the blood from the lungs to the arterial system.

Asthmatics not infrequently run a mild grade of *fever*. But so far as my observations go there is no exacerbation of the temperature at the time of the attack; or at least there is no such temperature change as would be expected in a violent anaphylactic reaction. The asthmatic condition tends to become chronic. A *nervous state* develops after if not preceding the asthma, and a habit of invalidism may be acquired. The disease rarely kills.

I have found *asthma and tuberculosis* to be commonly coexistent, but the diagnosis of the tuberculosis can be confirmed by the finding of tubercle bacilli in only about ten per cent of the cases. I think the tuberculous condition may be the primary etiologic factor and that from this result bronchitis and bronchial irritation with coughing of marked intensity and duration, asthma coming as a complication.

That a chronic inflammatory condition of the *bronchi* exists in some cases of asthma at least, I have demonstrated by *skiagraphs;* the bronchi cast a heavier shadow than do normal bronchi. Then too, the heavier bronchi in most cases plainly lead to the indurated lung areas.

The citation of illustrative case records follows:

*Case 1,* the study of which was responsible for the development of the Nonpassive Expiration Theory: male, age 49, plasterer. Except for syphilis in early life had always been fairly well till nine months before the time that I first saw him. He gave a history of an attack of severe pleuritic pains about eleven years before, and during the intervening years he had had some return of the pleurisy but these later attacks were never so severe as was the first one.

My history notes say nothing about his winter coughs and "colds." This is perhaps proof of my statement that even most physicians pay little heed to previous infections of the respiratory tract. But in a man who had been subject to pleuritic pains for years, there are almost sure to have been some annoyingly stubborn "colds" and coughs. About five months before I first saw him his health began to break rapidly.

During all the nine months he coughed very, very hard and after about five months began to notice that he was subject to attacks of labored breathing. This grew gradually worse until, at the time when I became his medical adviser, he was having two to five or more attacks every twenty-four hours. These paroxysms were typical bronchial asthma in every respect. They came on always with spells of hard coughing during which his face became reddish purple and puffed, and the veins of his neck were greatly distended. These facts are responsible for my present ideas. The lung findings were typical of asthma. In addition there was evidence of a small tuberculous area in one apex. The heart was moderately dilated and hypertrophied, but compensated. The pulse rate and temperature varied but slightly from the normal. Tubercle bacilli were present in the sputum which was ropy, tenacious and very difficult to free from the lips.

This case, I now think, was one in which syphilis probably played an important etiologic role by affecting the nutrition of the various tissues of the body especially of the heart, lungs, and bronchi. I did not at the time attribute the importance that I would today attach to the diagnosis of syphilis. The lues may have been responsible for an irritable condition of the bronchi or nerves, and hence partially responsible for the cough. This patient showed a marked grade of arteriosclerosis for his years. The tuberculosis, however, was sufficient to cause a severe bronchitis. The cardiac condition probably came directly or indirectly from the lues. The patient had three important factors for asthma—a cardiac condition, a bronchitis, and a cough.

The attacks came on day or night with but little advantage in favor of either and were the most severe I have ever witnessed. He later succumbed in an attack. The treatment and results of this case will be considered in another chapter.

*Case 2,* male, 36 years of age, had had asthma all his life. Father and mother both had asthma although they lived to advanced years. This patient had attacks periodically, usually at seasons of the year when climatic conditions predisposed to respiratory affections. Attacks followed hard spells of coughing. He was slender with a long narrow chest and the usual findings of asthma.

*Case 3,* merchant 23 years of age, single with family history good. When about fifteen or sixteen years of age he developed a pulmonary condition which was thought to be tuberculosis. He lived in a tent for the better part of a year and apparently completely recovered. A year or two later he went to college and

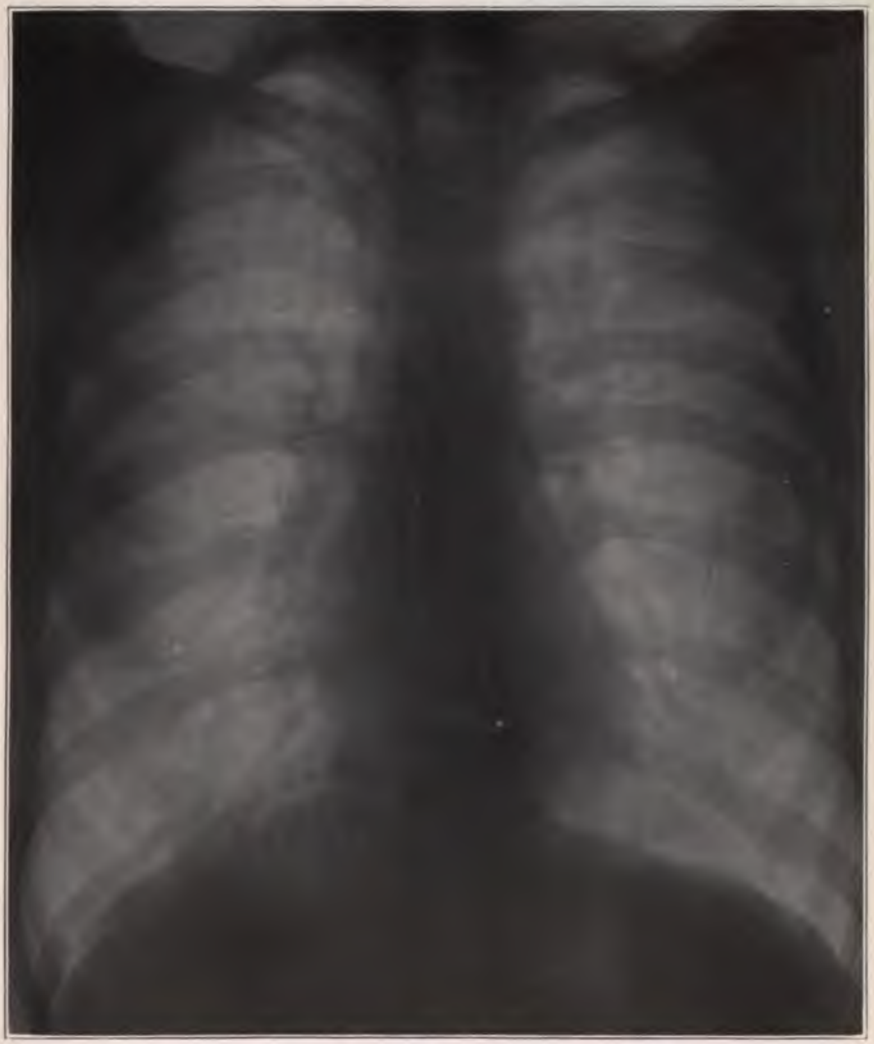


Fig. 30.—Roentgenogram of Case 19, Chapter XX. The special features of this picture are the prominent bronchi, showing induration; the diffuse shadows throughout the lungs, indicating tuberculosis; small tent-like raised areas in the diaphragm, indicating pleural adhesions; and the large right heart.

there played football. During his second or third year he received an injury in the early part of the football season which kept him out of the game and out of practice until the last game of the season. This contest was one which called forth the best efforts of every man. My patient was captain of the team and exerted himself to the utmost. He was taken out of the game in a serious state of exhaustion and remained all of the succeeding night in such a condition that his life was all but despaired of. As he recalls the events, his worst complaint was the difficulty with which he breathed. I take it that no one will dispute the diagnosis of a serious cardiac dilatation.

Following his recovery from this condition he took "cold" and developed what was probably chronic bronchitis and pulmonary phthisis. At any rate, the coughing was severe most of the time for months, following which came the asthma. In the chest were signs of bronchial catarrh and findings in the apices indicative of an early stage tuberculosis.

I hold that the cardiac and blood vessel strain plus the tuberculous condition which rendered his bronchial tubes subject to "colds" were the essential factors in the cause of his asthmatic dyspnea. Had he had only one of these conditions he might not have become asthmatic.

*Case 4,* farmer, age 45, single with family history good so far as could be ascertained, had suffered from asthma for perhaps ten years. The attacks were most severe when the season rendered respiratory affections most likely. He was particularly prone to "colds" and coughs and had been so for years before he developed asthma. Some ten to fifteen years before I saw him, he had undergone a very severe cardiac strain. He had gone hunting and shot a wild turkey. It appeared to be mortally wounded so he dropped his gun and ran after it thinking to catch it would be easy.

The task was more than he had anticipated; he was a man of much "stick-to-it-iveness" and as he expressed it he "chased the turkey all forenoon before catching it." As a result he was so exhausted that it required hours for him to recover. Here again was probably a cardiac dilatation. It is not difficult to imagine a more or less permanent injury to the right side of the heart, especially an injury which would simply allow a damming of the blood more readily than would be allowed by a wholly normal right heart. The cause of the bronchitis I was never able to prove. The disease, however, cleared up rapidly after the nose and throat were put in as good a state as possible and after the administration of some stock catarrhal "bacterins." Probably the nasal condition was primary to the bronchitis.

*Case 5*, female, age 44, inclined to slight obesity, had always enjoyed excellent health until eight or ten months before I saw her. At that time she caught a "cold" which caused her to cough a great deal and very hard. But after a number of weeks she apparently got well. Then about six weeks before I saw her for the first time she was thoroughly drenched by a cold rain and there resulted a second very severe "cold." The coughing with this was extremely hard. The infection invaded the bronchial tubes. After about six weeks of violent coughing she developed some dyspnea and this soon became of an expiratory type. She had been in the attack about twelve hours when I saw her. In this case I was not able to ascertain whether the heart was playing much part or not, but the patient is inclined to have a surplus of adipose tissue. Perhaps there is a sufficient layer of fat on the heart to cause some embarrassment therefrom. The pulse would indicate this and perhaps the sounds give further proof, but I plead an inability to decide definitely. The skiagraph shows indurated bronchi and enlarged right heart.

Here is a person who had been a victim of bad "colds"—an infection of the respiratory passages for months—and had certainly had as good an opportunity for an anaphylactic reaction at one time as another and yet the asthma came only after five weeks of suffering and after many extremely severe paroxysms of coughing. She has had one or two slight attacks of dyspnea since and always after considerably greater exertion than that to which she is accustomed and after some coughing. This, I think, tends to implicate the heart to a certain extent.

The cause of the bronchitis I was unable to decide upon. The physical state of the patient and the absence of any positive findings of tuberculosis in the lungs makes one doubt that it was a primary factor. Since writing the above the patient has returned with another attack of dyspnea. This, like the previous ones, came on after a bad "cold" and severe coughing. After the signs of the "cold" disappeared she was put on a strict diet designed to cause her to lose weight. She lost fifteen or more pounds and her breathing became labored less easily than formerly.

*Case 6,* female, age 30, has had hay fever for ten years, during the last three or four of which she has also had asthma. An attack of asthma with her does not develop until there is a general spreading of the irritation and inflammation. She is conscious of the gradual involvement of the trachea and bronchi. As this part of the respiratory tract is involved, the coughing also increases in frequency and violence. After about ten days the asthmatic dyspnea may develop. During the last two autumns, however, the hay fever has been held in check so successfully that no sign of dyspnea appeared. This case has been one that indicated to me that anaphylaxis produces asthma by the irritation and inflammation which it produces rather than by its effect upon the bronchiolar muscle.

*Case 7,* female, age 56, has been subject to hay fever and coryza symptoms for years; she says she has had these catarrhal manifestations as long back as she can remember. She has always had much coughing and sneezing and excessive secretions from the nose and throat but nevertheless she has been rated a strong healthy woman. The nasal condition was improved a few years ago by cauterization of sensitive spots of the nasal mucosa.

Last winter she was operated for a pelvic condition and the recuperation was slow. A "cold" supervened and a severe bronchitis followed. After some months of this she developed dyspnea, especially at night. Several of the attacks became very severe and of the expiratory type. Her coughing spells are very strenuous and impossible to control, lasting sometimes for as much as one hour or more; and with these the breathing is prone to be difficult. At the present time her bronchitis and cough are improving and the dyspnea is inconsequential. A recent attack came on with but little coughing and after a period of worry about her eyes. There were hemorrhages, however, in the conjunctivæ from the coughing.

*Case 8,* female, age 30, good physique, during early life was "puny" and subject to frequent "colds" and coughs. Undoubtedly a tuberculous condition existed. In recent years she has gained in weight and is plump. She is still subject to winter "colds." She is employed in her father's mill and the dust and smoke cause bronchial irritation and aggravating coughs. If the coughing endures a considerable period or if she is submitted to undue physical exertion she may develop asthmatic dyspnea.

Not long since she was in a train which passed through the tunnel and the car filled with smoke. This irritated her respiratory passages and caused her to cough, choke, and breathe with difficulty. Asthmatic breathing developed. But as she had been instructed how to breathe, the attack lasted but a half hour or even less. If she is careful to avoid "colds," dust, etc., and does not do unusual exercise, she has no signs of asthma. Treatment is apparently rendering her less liable to "colds."

*Case 9,* female, age 20, had a moderately active case of pulmonary tuberculosis. Tubercle bacilli were present in the sputum. This case had an unusually severe grade of asthmatic dyspnea and her coughing spells were about the worst I have ever known. She would have paroxysms of coughing which were absolutely uncontrollable and which would last, unless relieved by an opiate, until stopped from exhaustion. The asthmatic dyspnea followed the coughing spells.

*Case 10,* female, age 18, has practically the same history as Case 9,— she had tuberculosis with violent paroxysms of coughing followed usually by severe attacks of asthma. Both of these cases were studied intimately and carefully as they were both treated in the Sanatorium and my opportunity for studying them was unusually good. I have seen attack after attack come on, each always following paroxysms of coughing.

*Case 11,* male, colored, chauffeur, age about 36, had an attack of bronchitis which lasted a month. The coughing was very severe. I saw him in his first attack of asthma only. The dyspnea had developed gradually during the day or few days preceding his attack of asthma and culminated that night after some very hard coughing.

*Case 12,* female, age 35, housemaid, gave a history of frequent coughs and "colds" which dated back about eight to ten years while the asthma had existed but three or four. A fresh attack of "cold" would usually cause a choking up of the nose and throat and a wheezing in the chest which might continue for a day or several days without a severe attack of asthma. A coughing spell, however, might develop and an otherwise mild dyspnea would promptly pass into a severe paroxysm of asthma. Practically

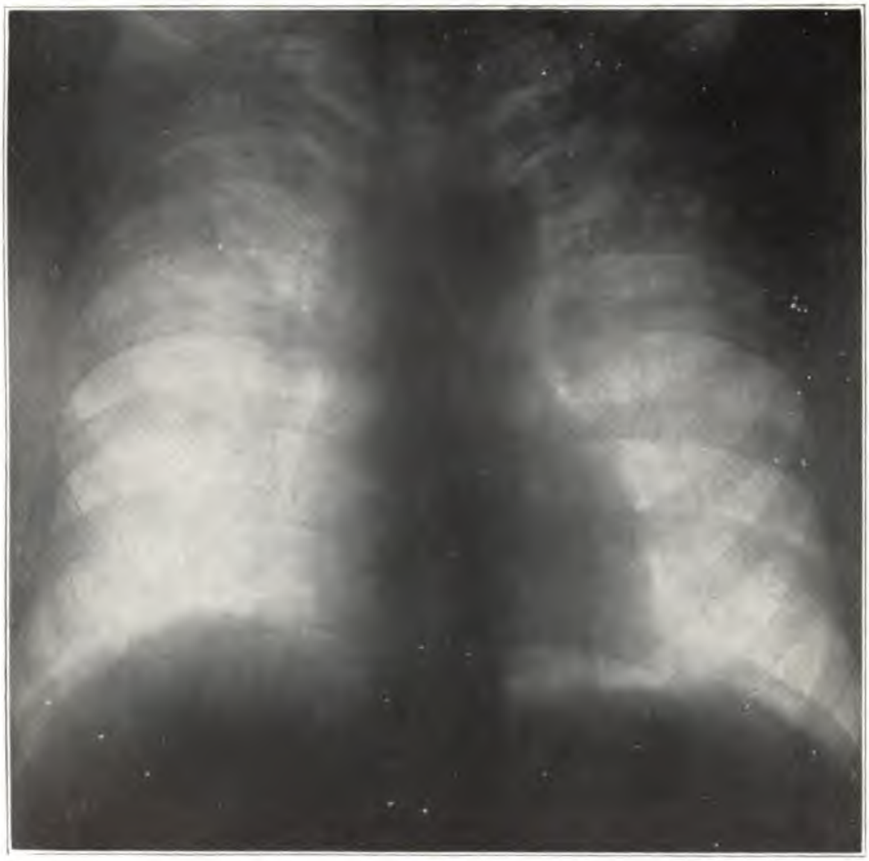


Fig. 31.—Roentgenogram of Case 18, Chapter XX. We note the dense shadows in each apex, the

every morning she coughed for an hour or more and was wheezy and dyspneic most of the forenoon.

Some friend of the patient had recommended a powder to be burned and the fumes inhaled. She used this nearly every morning and seemed to be relieved by it. Most of her severe attacks came on around 3:00 A. M. She maintained that she woke with the attack. She was a maid in my home and we often heard her coughing for some time before she called for help. It seemed to me that the secretions accumulated in the upper air passages during sleep and that for a time before she awakened the breathing was reflexly altered, causing some coughing and an effort to expel the mucus. This, plus the horizontal position, caused her to have some dyspnea so that she awakened badly frightened with the sensation of choking and inability to get her breath. From this stage it was usually but a step until she was using all the force possible on expiration. For days at a time she would be relatively free from asthma, then a "cold" would develop and she would be wheezy for several days before a real attack of asthma appeared.

Repeated examinations of the sputum did not reveal tubercle bacilli. But lung examination showed that both apices had positive induration. She was much under weight and her pulse rate was moderately accelerated. No other cause of the chronic bronchitis was found.

*Case 13*, male, physician, age 39, enjoys for the most part a very good state of health but has for years been subject to attacks of bronchitis which sometimes endure for many weeks. The dyspnea comes on with exacerbation of the bronchitis and usually there is more or less coughing, sneezing, and conscious breathing. He has had a considerable amount of operative work and other treatment directed at his nose with little or no benefit to the asthma symptoms.

One brother succumbed to tuberculosis and the left apex of the patient showed positive induration. On attempting to demonstrate just where the signs were most pronounced in his chest, he effected at his own suggestion a prolonged forceful expiration. He believed that he had a chronic bronchitis somewhat localized in the left apex. During the acute exacerbations it spread throughout the bronchi. Physical exertion seemed to have something to do with bringing on the attacks.

This case, I think, is one which illustrates a very important element in asthma; namely, that a tuberculous focus in the lungs may cause a mild, chronic localized bronchitis; the infection in the nose exacerbated by every slight weather change supplies bacteria by direct extension or by the blood or lymph to the bronchi, thus keeping up chronic bronchitis.

*Case 14,* is a woman 49 years of age, very obese, who has enjoyed good health until the last four months, during which time she has had a severe "cold," bronchitis, and cough. The coughing was especially severe and straining. Following severe spells of coughing or exercise, she suffered from labored breathing—a simple dyspnea. On examination, loud wheezing râles were heard at all parts of the chest. The râles were heard particularly on expiration. The nose was negative except for slightly enlarged turbinates. This patient I consider to have been in a preasthmatic state. Had the bronchitis and coughing continued with sufficient intensity and duration, true asthma would eventually have developed.

*Case 15,* male, 32 years of age, gave a history of having had bronchitis for four years, during the last two of which this was complicated with asthmatic dyspnea. The bronchitis and asthma were consistently more serious in the winter. Quoting from my notes, "Typical attacks of asthma come on usually about 11:00 to 12:00 P. M. and get better about 1:00 A. M. Then about 3:00 A. M. there is a recurrence lasting about 30 minutes; about 4:30 there is another mild paroxysm lasting only about 15 minutes." He says he awakes coughing, and shortly begins to wheeze and breathe with difficulty. Then the expiratory dyspnea quickly follows.

On examination, indurated areas were found in the right apex and in the right base posteriorly. On easy breathing, few or no râles are heard. But the râles become loud and prominent when the patient is instructed to cough or to expire forcibly without coughing.

*Case 16,* female, 42 years of age, wife of physician, complains of pain in right side in region of liver, paroxysmal attacks of expiratory dyspnea, and an aggravating cough. The focus of irri-

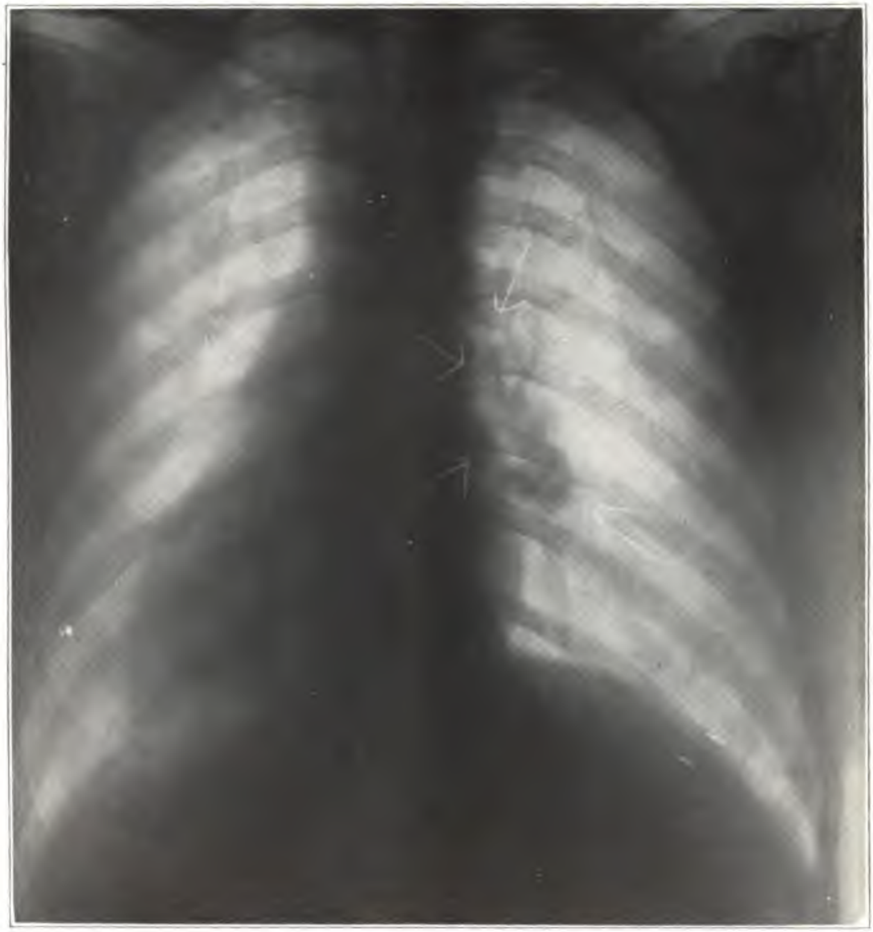


Fig. 33. Roentgenogram. This picture displays enlarged bronchial lymph nodes in the

tation responsible for the cough is in the chest. She has for perhaps 30 years been subject to bronchitis and for 10 years to asthma. She has attacks usually after coughing or exercise. She said. "If I sit real quietly I get better, but if I stir around much my breathing gets worse. I have more bronchitis and more asthma in damp bad weather." For a year or thereabout she has been subject to pain, cutting in character, in the region of the gall-bladder. These spells of pain have a tendency to aggravate the breathing.

On examination, an area over the gall-bladder was found to be tender. Later an operation proved the correctness of the diagnosis of gall stones. Sonorous râles were heard in the bronchi, the right apex showed definite signs of induration and the right base in axillary line signs of pleurisy.

*Case 17,* female, age 57, has been asthmatic since about 10 years of age. Some time during her ninth year she was caught in a snow storm experiencing extreme exposure, after which developed a severe "cold." The coughing she says was very strenuous and after a time she became asthmatic. During the last five years she has been less asthmatic than formerly. Now she gets around fairly well except when she has a "cold." When this comes on, the breathing does not immediately become asthmatic. But after about two days she becomes "wheezy" and somewhat dyspneic. Breathing gets to be a laborious worrisome process. Then after periods of coughing, especially, either after lying down, or after exertion, the dyspnea may become of an asthmatic character.

Examination reveals a typically emphysemic asthmatic chest, sternum high, ribs approaching a horizontal course, right heart large, diaphragm low, respiratory murmur indistinct and anterior posterior diameter greater than lateral dimension. The roentgen ray plate shows tuberculous foci in the lungs.

*Case 18,* male, age 49, has had asthma for but two or three weeks. Seven years ago he had well defined pulmonary phthisis. This improved in the next few years. But for three or four years past he has been subject to frequent "colds" and coughs. In December, 1915, he developed a respiratory tract infection which was diagnosed as "grip." This caused a considerable amount of very hard coughing. He had himself observed that there was a distinct relation between the paroxysms of hard breathing and those of coughing—the former following the latter. He had also observed the more he tried to force air out of his chest, the more difficult expiration became.

On examination it was found that the sonorous râles were heard at all parts of the chest. Both apices of the lungs were found to be indurated; the area of the aorta was decidedly enlarged, there was a tracheal tug and the impulses from the aorta could be felt in the suprasternal notch. Roentgen ray pictures confirmed the diagnosis of fibroid phthisis of the apices and a dilated aorta. It also showed a positive induration of the bronchi, especially those of the apices. Probably tuberculosis and syphilis both were important etiological factors in this case.

*Case 19,* female, age 31, up to five years ago had suffered much from asthma. A change of climate had given her complete freedom not only from asthma but from all respiratory tract infections. From about the time of puberty until the sojourn to another climate she had rarely been free from catarrhal affections of the respiratory system, during which she coughed a great deal. About three years after the onset of the coughs and ''colds'' she began to have dyspnea and this soon became asthmatic in type. The coughs and ''colds'' and likewise the asthma were most severe when the climatic conditions displayed sudden changes. A diagnosis of tuberculosis had not been made, but she was much under weight during this time of active trouble. Hypertrophied turbinates were removed without improving the asthma. Removal of the appendix and the doing of some needed surgery in the pelvis did not prove to be beneficial so far as the pulmonary condition was concerned.

On returning to the middle west, she began to have manifestations of a catarrhal involvement of the air passages with some difficulty in breathing. This, however, did not get to be of a typically asthmatic character. The usual findings of asthma existed and some small phthisical areas were suspected and later proved by stereoscopic plates. The bronchi showed with unusual prominence.

*Case 20,* female, age 76, complains of asthma which she has had for 10 years. Catarrhal manifestations preceded the asthma by "years and years." She is obese and the findings, type of breathing, and all were typical of asthma.

*Case 21,* female, 39, well nourished, gives a history of having suffered two years previously a severe attack of "grip" which became complicated with bronchitis. The coughing with these was very strenuous. The "grip" and bronchitis hung on tenaciously and some months later she began having a dyspnea which developed into asthma. The condition eventually improved, but now whenever she gets a "cold" she is liable to have asthmatic dyspnea. Her attacks may be precipitated at these times by getting irritable or excited. Usually, however, there is heavy straining coughing before the attacks come on. She breathes easiest sitting. She has noticed that if she breathes deliberately without muscular effort on expiration, the intensity of the dyspnea decreases.

The patient is robust and florid in appearance. Rhonchi are heard at all points of the chest especially during expiration. The nose was found to be negative. This case was diagnosed by a worthy confrere as "nervous asthma."

*Case 22,* female, age 29, for four years has had severe winter "colds" lasting practically the entire winter. In much of this time the coughing has been very trying. The past winter especially, the coughing has been very hard. Often she has coughed nearly the entire night. After these paroxysms she is unable to lie down because of asthma. With this there is loud wheezing. After a period of quietude, free from coughing, the breathing returns to normal.

Examination finds evidence of double pleurisy and slight induration of both apices. Tubercle bacilli have not been found in the sputum but the patient is probably tuberculous.

*Case 23,* female, age 56, has been asthmatic for four years. The labored breathing began to be manifest some three or four years before it finally became asthmatic. The history of "colds" and cough goes back much farther. Around ten years of age she had measles complicated with a severe bronchitis or possibly a pneumonia. She remembers that she was very ill and that a "cold" and cough lasted for weeks after the measles disappeared. She is not sure that she had severe "colds" each subsequent winter, but she says "colds" and coughs became common with her. Examination revealed an emphysemic chest, mild bronchitis, bronchophony and increased pitch of both apices, severe pyorrhea and a nasty nasal catarrh with some sinus involvement.

*Case 24,* female, 35 years of age, housemaid, has been asthmatic for about four years. She has had a marked tendency to "colds" and coughs for perhaps ten years. At times the cough becomes extremely severe. She was inclined to ignore the past history of the respiratory tract catarrhs until questioned specifically about them. Every fresh "cold" brings on the asthma. She is thin and there is evidence of bronchitis. Both apices show bronchophony, dullness, and high pitched breathing. The rhinologist reports hypertrophied middle turbinates, the shrinking of which improved the symptoms, but did not cause them to entirely disappear.

*Case 25,* female, age 48, gives a history of a very severe "cold" at 20 years of age. During subsequent winters she was rarely free from "colds,"—perhaps a winter now and then would be passed without them. Sometimes the "cold" began in early winter, lasting for weeks, only to be immediately followed by another. There has been considerable coughing with all the "colds." The bronchi were commonly involved in the later years.

Two years ago, early in the winter she had a severe "cold" which extended into the bronchi causing marked wheezing. This was followed by very strenuous coughing after which came the asthma. She does not remember how long the severe coughing lasted before the breathing became asthmatic; but she is sure that the attacks this winter have come on with much less coughing. She said, "After I start coughing, it feels as though my throat is swelling up inside and breathing soon becomes difficult." Lately she had a sneezing paroxysm lasting a number of minutes. Following this came dyspnea. An examination reveals that this patient has pyorrhea, hemorrhoids, an old operative hernia, and a tuberculous lesion of the right apex. The rhinologist reports that she has a hypertrophied middle turbinate and a mild sinusitis.

*Case 26,* male, age 20, has mild asthma. From his mother the information is obtained that he had had pneumonia during his first year, measles complicated with bronchitis at four, and whooping cough for months at six or seven. He has always been subject to bronchial catarrh with every "cold" and these have been fre-

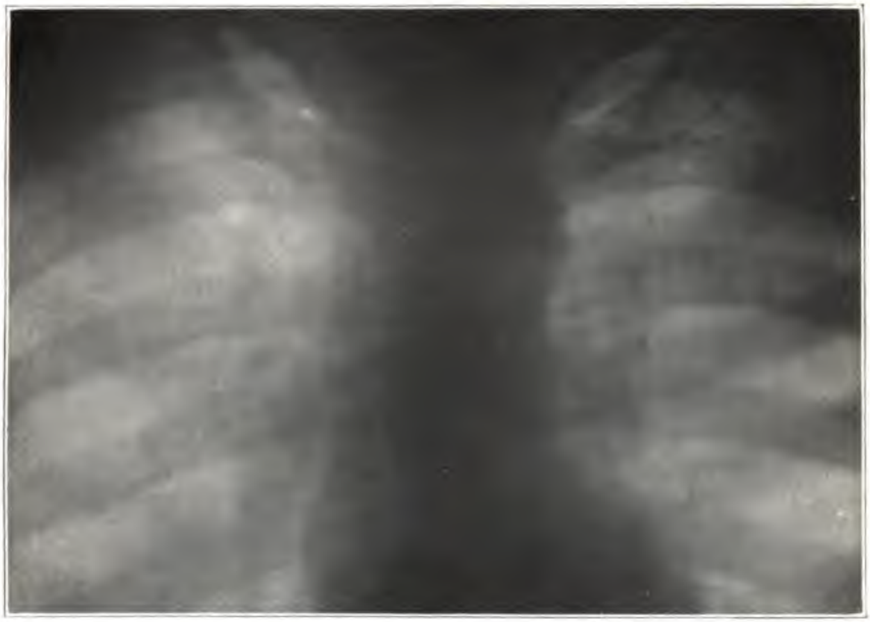


Fig. 33.—Roentgenogram. The enlarged bronchial lymph glands are also the prominent factor shown in this picture. They are represented by the dark shadows about both hila. The left apex also has some pronounced shadows, indicating pulmonary tuberculosis. (Courtesy of Dr.

quent since the time of the measles and whooping cough. About his sixteenth year or a little later, he began to have wheezing sounds in the bronchi. Although he had little or no dyspnea, his condition was diagnosed as asthma and sometime later one tonsil and his adenoids were removed and some operation was done to his nose. Little or no good was accomplished, however.

About ten days ago he was taken with a severe "cold" accompanied with extremely hard coughing. This continued for about a week and then he observed a decided difficulty in breathing. The dyspnea did not get to be typically asthmatic in character. An examination reveals dullness, high pitched breathing in left apex extending downward including the area about the larger bronchi. When breathing quietly, there is no sign of bronchitis, but a few deep breaths, especially putting force on expiration, brings out coarse rhonchi, particularly on expiration. Exercise or excitement of any sort tends to produce dyspnea.

*Case 27,* male, 28 years of age, railway mail clerk, has for the past year been subject to mild attacks of dyspnea occurring commonly around 1:00 to 2:00 A. M. While the paroxysms are usually not severe, they are nevertheless sufficient to cause him to arise and remain up for the greater part of the morning. The immediate history is as follows: One year ago he took a severe "cold" which was very slow in getting well and which produced a great amount of hard coughing. He got better in the fall, but during the winter he had two attacks of "cold" or grip which were again slow in leaving him. These were also accompanied with much coughing. Sometimes in the early winter he went through the St. Louis tunnel and the door of his car not being closed tightly, he breathed air, overladened with train smoke, for a considerable time. This produced heavy coughing and choking and his breath seemed to be absolutely cut off so that he neither could get air into nor out of the lungs.

He was three or four hours recuperating from the attack. It seemed to him that it abated only after he had become too fatigued to make further effort to breathe. He has observed frequently that dyspnea comes with hard coughing. He has also noticed that when his nose stops up, which occurs on slight provocation, his breathing becomes altered to such an extent that he is conscious of it; it causes him much annoyance and irritation.

After this endures for a time he finds that his breathing becomes labored.

On examination the breath sounds are found clear. There is some evidence of slight induration in the apices. The dullness over the right heart extends an inch to the right of the right sternal margin.

He was asked to breathe deeply but slowly. The respiratory note was clear. He was next asked to inhale quickly and forcibly, exhaling slowly and easily. There was no change in the breath sounds. He was then asked to inhale deeply and slowly and to exhale quickly and forcibly. With the first forcible exhalation a sonorous sound was heard over the bronchi. This appeared to increase slightly with each expiration until after perhaps a dozen respirations, the sound developed a distinctly sibilant character. This series of experiments was repeated and my findings were confirmed by Dr. W. M. C. Bryan and Dr. J. W. Marchildon. Dr. Bryan found in the nose a septum deflected to the left with a much hypertrophied middle turbinate attached to it.

*Case 28,* male, age 28, cabinetmaker, was well and strong until September or October of last year when he developed a "cold" and coughed "awfully hard" so that the neighbors a block away could hear him. The cough both day and night was worse on lying down. But he kept on working. Many times he would cough incessantly for perhaps four hours before he could stop. Along in January he began to notice wheezing. In March dyspnea began. Then in April he had the first very bad asthma attack and had to call the doctor. He coughed very hard before the attack came on. He has had four real hard asthma attacks. Each came on with hard coughing. He complains of pain in liver region with the hard coughing attacks. He gets out of breath on walking from which an attack of asthma may come. He has had a few attacks after eating. He sweats badly during attacks.

Examination reveals mild pyorrhea; induration right apex; wheezing and sonorous râles all over both chests, especially in expiration; pupils react sluggishly; tongue protrudes to left; left cremasteric reflex absent; some slight general adenopathy; 10 to 15 pounds under weight. He was suffering some asthma during the time he was in the office. The wheezing was most marked on expiration, being accentuated by a deep forceful expiration.

Forceful complete inspirations and slow passive expirations for a few minutes greatly decreased the intensity of the sounds.

*Case 29*, male, age 17, was seen first one year ago. He gave a history of having taken a severe "cold" 18 months before and of having coughed a great deal ever since. The spells of coughing came in paroxysms lasting usually for an hour or more once or twice each day. He had had one attack of rather severe dyspnea at the time he first consulted me. He was warned at that time of the danger of his condition developing into asthma. At the time of his second visit he gives a history of repeated asthma attacks coming on usually after periods of severe coughing. Usually about two hours after retiring a violent paroxysm comes on which lasts about an hour. The breathing gets dyspneic in 10 to 15 minutes after the cough starts. The cough ceases when he expectorates thick viscid mucus and the irritation in the respiratory tract abates sufficiently to allow the cough reflex to be controlled. Within 10 to 15 minutes after the coughing stops the breathing gets comparatively easy. He is compelled to sleep in a reclining position. He has also observed that exercise or undue excitement tends to precipitate the asthmatic dyspnea. Quoting him, "If I can keep quiet, not exercise, and avoid coughing, I can be fairly free from asthma, but when I hurry or cough hard, I'm sure to get asthma."

On examination the patient was found to be thin, habitus phthisicus in type, sternum high, chest irregular in contour, muscles of chest prominent. The arteries were unusually palpable for his age. The gums showed pyorrhea and there were some decayed teeth. The laryngologist, Dr. W. M. C. Bryan, reported that the nose is narrow, both middle turbinates being in contact with the septum; arch of palate is high and narrow; moderate sized adenoids are present; and there is evidence of the spheno-ethmoid cells being infected.

The examination of the lungs shows some positive induration in both apices,—difficult to outline readily because of the bronchial noises. The breathing is slightly labored, expiration being noticeably prolonged over inspiration and made with apparent muscular effort on the part of the abdominal muscles. The breath sounds are sonorous in character, louder over the area of the left larger bronchi than elsewhere; louder on expiration than on inspiration; and louder toward the end of expiration than at any other time.

He was instructed to inspire quickly and deeply and to expire quickly and deeply for fifteen times. The sounds became more prominent with both inspiration and expiration, but those on expiration were affected most markedly; after a few breaths the sounds were as though the lungs contained small whistles and more and more of them were being blown upon with each succeeding expiration. The whistling piping râles with something of a moist character were present by the hundreds. These changes came about rather promptly but were gradually increased till he was told to cease forceful expirations. The breathing was growing decidedly asthmatic in character and the patient was showing evidence of distress. He was asked to inhale in the same way as before but to exhale slowly and easily without an attempt to make it complete. The whistles left promptly and the noises gradually disappeared so that after a few minutes, perhaps after 20 to 40 breaths, a physician who had not previously listened to the chest would have recognized only a slight bronchial râle coming probably from a collection of mucus about the bifurcation.

He was then allowed to breathe at his own dictation; and so far as could be told inspiration and expiration were both being done in a normal way and in normal times. He stated that his breathing was easier than it had been all day and that he was breathing comfortably.

The observations given above were concurred in by Dr. Bryan, who agreed in every particular with me.

*Case 30,* male, boilermaker, age 32, has had asthma for about two weeks. He was in good health until about five months ago, when he began to have a hacking cough and was not feeling as well as usual. But there was no serious decline in his physical condition, though he had had a number of very hard coughing paroxysms, until about one month ago. At this time the cough and amount of expectoration increased greatly and he began to lose weight. The asthmatic dyspnea had its origin about two weeks ago and continued in a severe grade for approximately a week. It has been manifest but little during the past seven or eight days. He has been using alcohol and cigarettes to excess.

On examination it was found that he had slight evidences only of asthma—there being some high pitched sonorous râles in left base without sign of induration of the lung tissue. As he had had comparatively little asthma I felt that it was wrong to ask him to breathe so as to increase the asthmatic findings. In the right apex was dullness, high pitched breathing and bronchophony, indicative of a tuberculous focus. The gums showed serious pyorrhea and one gland anterior to the angle of the jaw on the right side was about two cm. in diameter and soft. The reaction of the pupils was sluggish; the Romberg reflex was positive; the left knee jerk was much weaker than the right; and the solar reflex on the left foot was not normal. An infection of the gums, tuberculosis of the lungs, and syphilis of the nervous system, it seems, are the elements primarily responsible for the asthma in this individual.

*Case 31,* female, housewife, age 27, has been asthmatic for 18 months. Up to 16 years of age she enjoyed the best of health, according to her own statement. Her mother, however, says she has coughed practically her entire life. At 16 she developed some nasal abnormality which caused her physician to send her to a rhinologist who operated upon her nose and tonsils. Shortly after the operation she lost weight, going down 25 pounds in the course of a few weeks. From this time on she has never been free from respiratory tract catarrh. She has had several nasal operations and has also been treated for pulmonary tuberculosis in a clinic of one of our better medical schools. Within the past eight months a suppurative condition of the sphenoethmoid cells has been discovered and operated with but little effect upon the asthma. The nose is not entirely well but the rhinologist reports that the discharge is inconsequential and that the nose is not sensitive. Treating the nose has little if any influence on the asthma.

During the past eight or ten years she has been troubled a great deal with paroxysmal sneezing and coughing—the coughing enduring sometimes incessantly "for hours." The first spell of asthma came on gradually and slowly. For the past one and a half years coughing has been prone to bring on asthma. Exercise may also precipitate the attacks. Excitement and nervousness will do the same. She has grown very nervous in recent years. The fears of an attack are very pronounced. Within the past year she has taken on weight so that now she is plump, weighing perhaps 10 pounds more than she should.

The findings on examination are negative except for the typical asthmatic condition in the lungs. The emphysema is moderate. The noises are not loud as the amount of air entering the chest is markedly reduced from normal. Inspiration is short and jerky and expiration is prolonged, muscular, and ineffective. The râles are sibilant, short in duration and very high pitched and squeaky in character.

She was instructed to stand, extend the arms lateralward and bring them forward slowly, exhaling easily and passively in the meantime, and then to throw the arms rapidly backward inhaling fully and completely at the same time. After a few minutes of such drill she was conscious of easier respiration, and I felt convinced that there was a decided decrease in the number and intensity of the sounds. I think unquestionably the nose has been the prime factor in this case; probably a tuberculous focus in the lungs has helped to maintain a mildly inflammatory state of the bronchial mucosa. The coughing and sneezing have been of such marked intensity and duration, however, that an asthmatic state might have developed even in the absence of a bronchitis.

*Case 32,* female, age 78, has had bronchitis and nasal catarrh for 15 years. During the last six to eight years asthma has developed. There has been much hard coughing, during most of the period of bronchitis. At times the condition improves, but for a number of years now she has had but rare intervals in which it might be considered that she was fairly well. The paroxysms of coughing are at times uncontrollable and are prone to run into asthma. The horizontal position, exercise, excitement, worry, etc., are other factors which may precipitate an asthmatic attack. The chest is emphysemic in formation, hyperresonant, and on auscultation, many piping râles are observed, more marked on deep forceful expiration.

*Case 33,* male, physician, age 66, developed two years ago a heavy "cold" and bronchitis. After about four months, during which time the coughing had been very strenuous, he became asthmatic. The heart was prone to dilate easily and seemed to be an important factor toward promoting the asthma. An x-ray examination showed the presence of an aortic aneurysm. Typical findings of asthma existed.

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# CHAPTER XXI.

## THE CLINICAL HISTORY, PHYSICAL SIGNS, AND SYMPTOMS OF ASTHMA (Cont'd).

The *observations* presented in this chapter, it should be remembered, were written originally in support of theories, none of which had the essentials of my theory, and many of them differed widely from it. I am selecting those observations which tend to give the clearest clinical picture of asthma. Because of the great abundance of contributions on the subject, the number of selections are of necessity only a comparatively small percentage of those to be had.

Pescatore[1] has devised a *system of questions* to facilitate obtaining the histories of patients with asthma. Some may find it of use. Lack of space prevents its being given.

In regard to the part that *heredity* plays in asthma, Salter[2] says he found an inherited disposition in 84 of 217 cases; Berkart[3] noted it in 16 per cent; LaFétra[4] observed three cases which were asthmatic at birth. Drinkwater[5] gives the chart shown in an accompanying figure, of a family of asthmatics, one of the parents of which he thinks "was almost a heterozygous abnormal parent." There were 10 normal and 10 abnormal descendents which he says is in accord with Mendel's 50 per cent of each class in such cases.

In regard to the *age* at the time of the development of the asthma, Smith[6] reports 36 cases of which definite information was obtainable in 34. Of these, the attacks began before one year of age in 20 and before three years in 28. In Salter's[2] series of 225 cases, 11 became asthmatic before one year, 60 from one to 10, 30 from 10 to 20, 39 from 20 to 30, 44 from 30 to 40, 24 from 40 to 50, 12 from 50 to 60, four from 60 to 70, and one from 70 to 80. One-third of Berkart's[3] cases were asthmatic before 10 years of age. Sokolowski[7] found that in his series of 105 cases, 65 began under 10 years of age.

LaFétra[4] reported a series of 43 cases of asthma in children. In this series *characteristic symptoms* were reported to be *present* at birth in three cases, from birth to three months in two cases, from three to six months in three cases, from six to twelve months in three cases, from two to five years in nine cases, and from five to 12 years in 15 cases. Goodhart and Spriggs[8] report a series of 50 cases, all of which were under ten years of age. In Comby's[9] series of 75 cases, 56 began before three years of age. Wolf[10] says that the youngest case on record was 28 days of age.

In regard to *sex* and *color* in asthmatics, Lemann[11] reports that in a series of 7000 patients ill from various causes, 31 were asthmatics—14 whites and 17 negroes, 16 males and 15 females. Of the total number of 7000, 45 per cent were whites. Of LaFétra's[4] series of 43 cases of asthma, 27 were males. Goodhart and Spriggs[8] found that 31 out of 50 were males. Salter[2] says of 207, 138 were males and 69 females. Wolf[10] thinks asthma is nearly twice as common in males as in females.

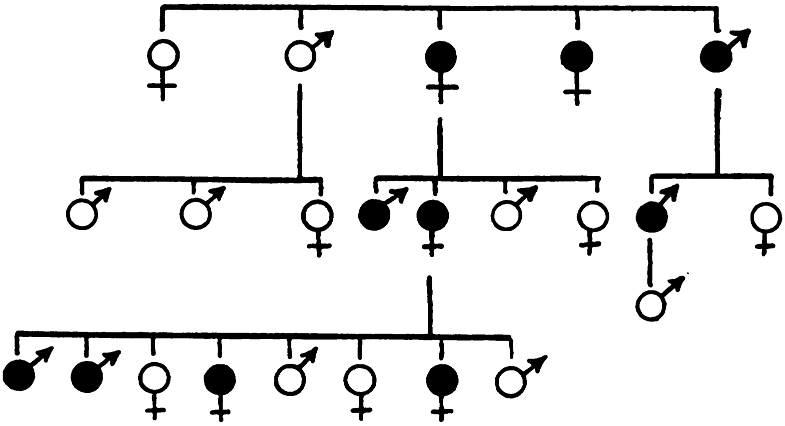

Fig. 34.—Drinkwater's Chart. In some cases of asthma there is unquestionably a hereditary base. The constitution for the asthmatic seems to be that for the tuberculous. Drinkwater found that half of the offspring of an asthmatic parent became asthmatic.

The Editor of the Therapeutics Department of the *Journal of the American Medical Association*[12] speaks of the *chronicity of asthma,* and says that the *onset* of the attacks is with slight dyspnœa and a hacking cough, but the cough he does not apparently emphasize as being more than an incident. He says the attacks vary in duration from an hour to perhaps several days. Johnston[13] reports an attack lasting for nine days.

Floyer[14] had most of his *returns in hot weather,* and they were likewise the longest. This may be accounted for in two ways, either the patient was a victim of so-called hay asthma, or he suffered from pulmonary tuberculosis, or he may have had the two conditions both of which are prone to be most severe in hot weather.

Bree[15] says *dust* may produce asthma and that it first brings on sneezing. And again, he says the paroxysms "supervene upon the milder effort to eject an acrid material by sneezing and cough." Bree refers in many places in his book to the association of *cough and sneezing* with asthma.

Osler[16] says, "The *cough* is at first very tight and dry and the expectoration is tenacious. *Emphysema* of the neck may occur during the violent coughing spells." Lord[17] says "Successive attacks over a period of days or weeks in the intervals between which the patient coughs and is short of breath are frequent." But more will be said later of the influence of coughing, sneezing, and of respiratory tract catarrh.

Whitby[18] reports a case which developed a *subcutaneous emphysema* during an attack of asthma. Goldschmidt[19] calls attention to the lack of *fever* and *cyanosis.* Mignion[20] reported that he had observed three cases of asthma which showed distinct *delirium* at the time of the *crisis.*

Salter[2] observed the *influence* of a prolonged *deep expiration* on the râles and sounds of the bronchi. He says, "I have long observed that rhonchi and sibilant *râles* are often audible during expiration, that they are frequently confined to the end of an expiration, not becoming audible till the expiration is half performed; that the longer and deeper the expiration the louder they are; and that the inaudible respiration of persons in apparently good health, particularly the old, may be rendered wheezing by making them effect a prolonged expiration. If you *tell a person with unsound lungs to wheeze he immediately effects a prolonged expiration,* as if he knew that that was the way to produce a wheeze. Now, the source of the sound—the plug of mucus or the inflamed tumid membrane—exists as much during inspiration as expiration; why then should the sound be present in the one and absent in the other? Moreover, I have noticed, (and this is a very curious fact) that when the breathing is inclined to be asthmatical the dyspnea may be aggravated, while on the other hand, the spasm may be broken through and the respiration for the time rendered perfectly free and easy by taking a long, deep, *full inspiration.*"

Talma[21] describes the characteristic *sounds* of asthma by saying that they are more pronounced in expiration and especially toward the end of expiration when they become somewhat higher in tone. The sounds he says are most pronounced over the larynx, trachea, and larger bronchi, and must be made in one of these localities; for they surely cannot be produced in the finest bronchioles. Campbell[22] also made the clinical observation that the wheeze is more pronounced on a forced expiration. He calls attention also to the distention of the chest.

Loeschcke[23] in some careful studies of the pathologic physiology of emphysema came to the conclusion that one of the first changes to come about was the development of a *kyphosis* in the dorsal region, increasing the anterior posterior diameter of the chest. The pressure above the diaphragm increases, he maintains, while that below the diaphragm is likely to decrease from loss of adipose tissue and stretching of the abdominal muscles and through enteroptosis.

Levy-Dorn,[24] Schlesinger,[25] Daly,[26] Krause,[27] Jamin,[28] and Warren[29] report *orthodiagraphic studies* of cases of bronchial asthma. These studies have shown a horizontal position of the ribs, increased intercostal spaces, a lowered flattened diaphragm, a low centrally placed heart and a diminished density of the lungs. Levy-Dorn especially called attention to the fact that the apex beat was likely to be in the sixth interspace near the left sternal margin, while the right side extended considerably beyond the right margin of the sternum.

Warren also made the observation that the *overdistention of* the *lungs* and associated phenomena remained for months, even though the patient continued during this time to be free from the attack. He accounts for this on the assumption that there had been a loss of elasticity of the lung tissue.

Von Strümpell[30] says the diaphragmatic *border of* the *lungs* is found to be lowered one or two costal spaces during an attack. Hoover and Taylor[31] have observed narrowing of the *costal angle* in inspiration during an asthmatic attack.

McPhedran[32] says of asthmatics, "The face is pale and anxious at first but soon becomes livid and swollen with protrusion of the eyeballs, and as the attack continues, the cyanosis becomes very great. There is a copious flow of nasal secretion that provokes sneezing. Profuse alarming perspiration breaks out and the extremities become cold. All these signs show the great *strain* to which the *right heart* is subjected." He also calls attention to the depression of the diaphragm.

Stäubli[33] discovered that the amount of the *tidal air*—that which is changed with each respiratory cycle—is greatly reduced in asthma. He explains this by saying that the air left in the lung—the residual air and the reserve air, the latter being that which can be expelled by a maximum expiration—is present in such amounts that the actual quantity which can be utilized is reduced, while the complementary air, that which can be drawn in at a breath above the ordinary amount inspired, is reduced to the minimum.

Lemann[11] reports that he makes it a routine practice to refer all cases of asthma to rhinologists for examination, and that as a rule, these specialists make negative reports regarding any *pathology of* the *nose and throat*. He comments on the frequency with which he meets *obesity* and asthma in the same individual.

Stäubli[33] discovered that the *viscosity* of the *blood* is increased in asthma. He also calls attention to the facts that asthmatics are emphysematous and that the right heart has excessive work to perform.

Salecker[34] examined the blood of fourteen asthmatics and found that during an attack and for a few days afterward, there was commonly a mild *leucocytosis*, with the differential count showing an increase of the polymorphonuclear leucocytes to 80 per cent and a decrease in the mononuclears and eosinophiles. His work was confirmed by von Hörstin.[35] In seven cases which he studied carefully, he found in the intervals between attacks polymorphonuclears 40 per cent, lymphocytes and mononuclears, 45 per cent and eosinophiles 12 per cent. During or shortly after the attacks he found an increase in the polymorphonuclears and a lesser number of mononuclears and eosinophiles. The latter were likely to be absent from the blood during an attack. He reports finding a higher percentage of eosinophiles in chronic cases than in acute cases.

Neusser,[36] Mandybur,[37] von Noorden,[38] and Fink[39] found that at the time of the attacks there was usually an increase in the number of *eosinophiles* in the blood. Von Noorden reports a case with 33⅓ per cent of eosinophiles of the blood during an attack, and five per cent during a free interval. Zappert[40] and Wolff[41] each reported the finding of about 10 per cent of eosinophiles in the bloods of asthmatics during the intervals of freedom from attacks. Coler[42] found a case of asthma with 25 per cent of eosinophiles in the blood. Billings[43] had a case with the leucocytes amounting to 8600, of which 53.6 per cent were eosinophiles. Herrick[44] reports a case with 57,000 leucocytes, 77 per cent of which were eosinophiles. Gabritschesky[45] found in three cases, 10, 22, and 16 per cent respectively. The case with 10 per cent averaged about two attacks a month, and the one with 22 per cent about two or three per week. Cabot[46] reports a case with eosinophiles ranging from 11 to 15 per cent.

Siebeck[47] has shown that *in emphysema* even with deep breathing there is *less oxygen taken up by the blood* than in normal lungs. Reinhardt[48] demonstrated that in emphysematous persons there is *less discharge of carbon dioxide* gas than in the normal lungs. Hoover and Taylor[31] confirmed this finding and say it is due to the dilated alveoli making interchange of gases more difficult.

Salter[2] says, "*Hypertrophy and dilatation of the right heart* has long been a well known recognized complication of asthma." He speaks also of "the small feeble pulse, the irregular faltering systole, the turgid veins of the head and neck, the occasional hemoptysis, the dusky skin," etc.

The Editor of *Progressive Medicine,*[49] however, has the following to say of the *heart:* "The special heart feature noticeable in the ordinary case of confirmed spasmodic asthma is its soundness and endurance. The recurring attacks are usually more damaging to the lungs than to the heart." Götzl and Kienböck[50] report having found two cases of asthma with hearts unusually small during the attack as shown by the fluoroscope. They explain this by saying it is probably due to the heightened pulmonic pressure while the paroxysm continues.

Gilbert and Villaret[51] found three cases of asthma who complained of decided *pain in* the *liver* and in whom there existed for a short time some slight jaundice and other evidence of bile in the blood. They were at a loss to explain the pain. The liver was only slightly enlarged and the heart was negative. The disappearance of the pain, they thought, might be due to an atrophy of the liver cells. The swelling of the liver, the jaundice, and the pain were probably only the evidences of an overworked right heart.

Francis[52] found in 100 cases of asthma, 23 who had a *blood pressure* of 145 or higher, 74 with a pressure of 125 or higher, while in 18 the pressure was below 120.

Russell[53] found the *diameter* of the *radial artery* in an asthmatic paroxysm to be 2.2 mm. and after the attack was relieved by nitrites, the diameter was 2.4. Hare[54] was also convinced that the radial artery undergoes a contraction during an attack. Brown[55] in regard to this says, "The fixation of the chest which occurs in the attack must interfere with the diastolic filling of the heart and thus lead to a small pulse through diminished output during systole."

Störk[56] in 1857 observed with a laryngoscope that the *mucous membrane* of the trachea was markedly hyperemic during attacks and that the two conditions passed off together.

Freudenthal[57] says of the *bronchial mucosa* of an asthmatic when seen through a bronchoscope, it "will be found more or less swollen, often to such a degree that the cartilaginous rings cannot be seen at all. This swelling is sometimes so pronounced that it bulges into the lumen of the tubes, and for a moment one may be in doubt whether one is in the trachea or esophagus. In the smaller bronchi, this condition is even more pronounced, so much so, that occasionally, as has been pointed out before, the orifice of a smaller bronchus does not appear larger than the head of a small pin."

Heilskoy and Mahler[58] made 120 endobronchial examinations during the attacks for the purpose of applying adrenalin. They say, "The *mucosa* in all was found very red and swollen and during expiration and coughing, the lumen was seen to close up entirely." In the intervals between paroxysms the mucous membrane was found to be nearly normal. Others have made the observation that congestion and swelling exist during an attack and pass off as the attack diminishes.

Von Strümpell,[59] while admitting that there may be cases of pure nervous asthma, says, "In most cases of bronchial asthma, however, the attacks, as we have said, are only more or less sudden exacerbations of a condition which in the intervals is not perfectly normal. While ordinarily only the signs of a *chronic bronchitis* are present, often, associated with pulmonary *emphysema,* from time to time exacerbations occur, usually in the form of long continued asthmatic dyspnea, lasting for days or weeks." Of hay asthma, he says, "The symptoms consist in a very severe coryza, with burning of the nose and violent sneezing."

I quote from Abbott,[60] as follows: "In one of the writer's cases (a young American woman, aged 26) there was a slight ethmoiditis, with very slight hypertrophy below the left middle turbinate. She had suffered from *violent sneezing* for about six months (January to June) and at times *an annoying cough,* which had been diagnosed as *bronchitis,* had appeared. After operation the sneezing and bronchitis disappeared and did not bother until one year later when the right ethmoid became involved. She would admit no history of asthma but after a short trip on which she caught *"cold"* she had her first attack of *asthma.* She was seen two days later, when it was observed that her ethmoiditis was worse than when seen before the trip and she had a slight asthmatic wheeze. After operation this disappeared and no trouble has arisen in the eight months since."

Anders[61] and Dieulafoy[62] both hold the opinion that *bronchitis* frequently occurs in *asthma,* but that the former develops as a result of the latter; neither take any notice of the existence of a cough. Thompson[63] on the other hand, as has already been quoted, holds that cough is an essential etiologic factor in asthma. Middlemiss[64] reports a patient in whom bronchitis had existed since childhood and asthma for two years.

Mahomed[65] observed that one of his cases had the *attacks* brought on *by exercise.* This author also refers to *laughing* as playing an important part. Hoover and Taylor[31] say of one of their cases: "The case presented the usual type of emphysema with bronchitis and asthma. *Bronchitis* existed a year before admission but the asthmatic attacks only for a few months."

Goldscheider[66] refers to the importance of *cough* by saying that it is necessary for the patient to control his cough in order that he may be benefited by breathing exercises. Saenger[67] says, "Another important point is to teach the patient to control the tendency to cough, as the cough is liable to start the attack of asthma." Keiper[68] reports the history of a patient who caught a bad "*cold*" October 3, 1913. He coughed very hard and asthma developed November 30, 1913.

Koessler and Moody[69] say, "The carefully taken histories of the greatest number of asthmatics show over and over again the following facts: first, the first attack of asthma started after a '*cold*,' tonsillitis or *grip* of several weeks' or months' duration. Second, every subsequent attack or series of attacks is introduced by a new 'cold' or *bronchitis* coming on as a rule in the time of the year when the nasobronchial infections are prevalent. Third, a good number of asthmatics are subjects of chronic bronchitis from which they suffer more or less, even in the intervals between the attacks. Bronchitis is usually regarded as a concomitant affair of subordinate nature which develops secondary to the asthma."

Talbot[70] reports six cases of *egg asthma*. In regard to *Case I*, he says "*colds*" became common around two years of age, followed six months later by an urticarial eruption all over the body and a cough; the chest contained many medium and coarse musical râles scattered over both lungs, and he had considerable difficulty in breathing. The bronchitis lasted for about three weeks. During his period of immunization to egg, he again developed a bronchitis, which disappeared on leaving off the egg capsules. The author concludes that he established a definite connection between the *bronchitis* and the egg white.

Of *Case II* Talbot says, "At the age of fourteen months his adenoids were removed because of frequent '*colds*,' with some improvement, but as the 'colds' still persisted, the adenoids were again removed at two years. After that the character of the 'colds' changed, going down into the *chest* and he became *wheezy*. . . . . Since then the attacks have become asthmatic. The lungs were hyperresonant throughout with slightly prolonged expiration and occasional squeaks." The second day he became cross and the morning of the third day he began to sneeze, and a rash appeared beneath the skin. On the evening of this day he had an attack of asthma.

Nothing is said of the bronchitis, coughing, etc., in Case III. In regard to *Case IV,* Talbot says, the child had been gradually immunized to egg and "the asthmatic attacks in the meantime had grown less and less severe so that at the end of six months they had entirely disappeared. He was then *given* some of the dried powdered *egg* white mixed with cereal. A few minutes later his *lungs filled up* alarmingly and for the rest of the day he had marked dyspnea and coughing."

In regard to *Case V,* Talbot says, "It was decided to give him some powdered *egg white* not in capsules. Almost immediately after its administration he began to *cough* and at the end of five days, the cough had become asthmatic. The albumen was therefore given in capsules and the cough immediately stopped. Since then he has been entirely free from *asthma.*"

In regard to *Case VI,* I quote as follows, "He was *barrel-chested* and round-shouldered. His lungs were hyperresonant throughout, expiration prolonged and there were many medium and fine *squeaks* in both chests." I think these cases show that egg anaphylaxis produces swelling and edema of the bronchial mucosa, coughing and conscious respiration, which in turn cause asthma.

Quoting from Berkart,[3] "The disease is invariably preceded for an indefinite time by some form of *inflammatory changes* of the *respiratory tract.* It may safely be asserted that no one suddenly becomes asthmatic in the midst of perfect health. Some indeed declare, no doubt in good faith, that up to the moment of their first seizure they have never had a day's illness. It must, however, be borne in mind that the laity do not look upon a functional derangement or organic lesion which does not entail confinement to bed or a temporary incapacity from the pursuit of business or pleasure as illness.

" '*Colds,*' as they are called, '*sneezing fits*' or coughs, however frequent or protracted they may be, are generally regarded as still within the limits of health and are seldom suspected as the possible precursors of more serious mischief. Yet, if the histories of those seemingly exceptional cases be carefully scanned, it will be found that here also there is no exception from the rule.

Thus one gentleman was very positive that he knew not what illness was until he had become asthmatic. It was soon, however, elicited from him that shortly before this event his relatives had noticed, on the occasion of his attending his brother's funeral, the *distressing cough* from which he had suffered for a long time, and had anxiously entreated him to seek advice. Another, who was equally emphatic on the same point was quickly reminded by his wife how long he had been subject to a kind of cough which had always sounded to her like whooping cough and had greatly disturbed their nights' rest.

"Of the nature of those antecedents little is known from actual observation. All the information on them is derived from the reports of the patients who, when they first present themselves, have already been for years confirmed asthmatics; and although in these circumstances the alleged diagnosis can have no claim to strict accuracy, they may nevertheless be regarded as substantially correct. It appears that in more than 60 per cent of all cases, typical *asthma* declared itself during the first ten years of life and was promiscuously *attributed* to *whooping cough, measles, bronchitis,* congestion of the lungs, *pneumonia,* protracted *'colds,'* tonsillitis, croup, diphtheria and scarlatina.

"If more details of the manner of the origin can be obtained they amount to this, that the acute and specific symptoms had subsided, but that the *recovery* had been *imperfect; cough* and some *breathlessness* on exertion had remained behind and had persisted perhaps without attracting special attention until an intense dyspnea suddenly set in one night after a few hours' restless sleep. After the first decade, however, its development becomes less frequent and takes place in each of the second and third in about 15 per cent, beyond the fifth in only two per cent. In all of these it is assigned to colds, coughs, sneezing fits, hay fever, or other catarrhal affections, which, seemingly insignificant at first, had gradually gone from bad to worse, culminating at last into *asthmatic seizures.* Gout and rheumatism, which in some instances are said to have caused it, have probably no larger share in its origin than that they have supervened in the conditions above mentioned; but as their symptoms are more conspicuous than those of the chronic catarrh of the air passages, they are readily assumed to be responsible for the serious trouble that followed them."

After describing causes of the bad "colds" and infections of the nose, throat and bronchi, he says, "Notwithstanding a distressing cough and some oppression at the chest, the patients contrive, not, however, without some painful effort, to *follow* as far as possible their *usual avocations.* Their chief complaint is that every movement, especially going upstairs, tries their breathing, whereas their state is bearable when they are at rest. At last after a short and uneasy sleep, the dyspnea becomes excessive. The suffering hitherto experienced fades into insignificance with what it has now become. The inflammatory changes of the air passages which were regarded as a common 'cold' have thus developed into an attack of asthma.

"The *severity* and *duration of* the *attacks* vary according to the state of the lungs, the presence or absence of complications, and the length of time since the disease declared itself. It would seem that in some instances they are of mild character—consisting chiefly of wheezing which frightens the patients and perverts their respiratory acts."

Again quoting from Berkart, "The incessant cough which torments them makes no impression upon the impediment, nor does the copious frothy *expectoration* bring them any relief. A common complaint is that of *headaches* which are largely aggravated by the cough.

"*Organic lesions* of the bronchial mucous membrane are *never absent.* If the diagnostic signs of bronchitis are open to misinterpretation during the dyspnea seizures, there can be no room for it in the free intervals. There is the cough which is especially troublesome in the morning, and there are the sputa presenting the peculiarities previously described, scanty in the earlier, more abundant in the later stages of the disease. . . . . Hand in hand with this form of bronchitis goes generally emphysema."

Berkart reports the *clinical history* of one of his cases quite *in detail* as follows: "Mrs. C., age 37, with a history of *phthisis* on her father's side, had had when a child *whooping cough,* measles, and scarlet fever. She had also had, as she distinctly remembered, a marked disposition to 'colds' which were especially severe in the early summer. Menstruation began at the age of 13.

She married at 21 and has had five children, all of whom are alive.

"Fourteen years ago she had been seized with an attack of *bronchitis* which had confined her to bed for several weeks. Recovery had been but imperfect; her breathing had remained embarrassed and soon afterwards she had become subject to typical attacks of asthma. The bronchitis had frequently returned lasting each time for several weeks, during which she has been unable to leave her bed."

Salter[2] reports a series of *44 cases* giving the attributed *cause of* the start of the *asthma* in each. Such terms, however, are used as "inherited," "atmospheric conditions," "constitutional," "unknown," "spontaneous," "small-pox driven in," etc.; in one-half of the instances the cause is given as "colds," bronchitis and such like conditions. No mention is made of nasal conditions. In 10 of the cases where the start of the condition was thought to be other than "colds" and respiratory tract infections, the individual attacks were said to be initiated by factors which directly affected the respiratory passages.

On presenting these facts it is only fair to the present work to state that *Salter's theory* held asthma to be spasm of the bronchial muscles. Naturally his attention was not especially attracted to the question of coughs, "colds" and other factors which might produce an increased intraalveolar air pressure. Then, too, coughs and "colds," particularly in the winter time, were expected by the older generation, and unless prevailing to an excessive degree were not even remarked about. In spite of these facts, *75 per cent* of Salter's cases *gave* positive *histories of coughs and "colds,"* either acute or chronic.

In the appendix of his book, he gives in narrative style the *histories of eleven cases* of asthma. I quote freely from each of these case histories.

*In Case 1,* Salter describes how a hay fever subject became asthmatic. He has the patient describe his own case as follows: "I well remember the first attack of those symptoms which, now more developed and regular in their appearance, I recognize as my annual *'hay fever'* torment. I was a little boy eight years old; it was in the month of June and I was one of a hay making party. I was at the play work of hay making with my young companions, surrounded by new mown grass, when I was suddenly seized with all the eye and nose symptoms of hay fever—profuse lachrymation, swelling of the conjunctiva and lids, with intense ecchymosis well nigh blinding me, and *ceaseless sneezing.* I recollect that I was taken into the house by my elder companions and speedily recovered.

"It was, however, about the fifteenth year of my age before I was conscious of my annual infirmity—before I understood that at every early summer I was liable to sneezing fits if I ventured into the country; but from that time until the present, this tendency has been abiding, has manifested itself every year, and has always governed my habits and residence during the month of June and part of May and July. I have said I was eight years of age when I first suffered from hay fever symptoms; the liability was obviously intensifying as I advanced in life. I had not, however, then become liable to one of the most distressing elements of the complaint—*asthma;* for I think I must have been fully *twenty years* of age before that symptom was one of those which combine to constitute this singular complaint when fully developed. In my case, the malady was not established in all particulars and to its full force till about my twenty-fourth year; since then it has remained pretty much in statu quo.

"The amount of asthma I have at night very much depends on the sort of day I have had previously, and how I have conducted myself gastronomically: as one sneeze begets a paroxysm, and as one paroxysm begets others, so does a *sneezy day* beget a *night of asthma.* The excitement of the sneezing act seems to render the bronchial muscles peculiarly irritable and liable to take on spasm; the same is the case with violent *laughing;* indeed, much laughing, especially just after dinner, will often bring on an asthmatic spasm at once. A quiet day without much sneezing—when that rare luxury does occur—is often followed, even in the bad season, by an almost unasthmatic night."

This *patient,* we see, had been duly *impressed* with the bronchial *muscle spasm theory.* He probably was a physician. The important points in the above narrative are that this patient suffered several months yearly for 12 years with respiratory tract involvement before asthma developed and that the individual attacks followed paroxysms of sneezing, coughing, laughing, exercise, etc.

*Case 2* seems to be an example of the cases where little or no reference is made to the coughs and "colds." He, however, states the following: "The first attack of an asthmatic character that I can remember having experienced was when I was recovering from *measles* at the age of eight or nine years. This attack was speedily relieved by the application of mustard poultice to the chest.

"I can remember having occasional fits of dyspnea at night from this time till the period when on commencing the study of medicine, I recognized them to be asthmatic. At that time I believed them to be the consequence of *catching 'cold.'* Exposure to cold when heated, as in getting out of bed on a cold night, I have found a frequent cause. The attack ceases on the expectoration of pellets and what seems to be casts of the air tubes, composed of a rather tough, gelatinous, transparent grayish substance.

"I remember one attack a good many years since, apparently induced by immoderate *laughter,* which disappeared after 10 or 12 hours with the usual expectorations." Although this physician did not directly attribute his asthma to "colds" and coughs, we can see that they must have certainly played an important part in his malady.

*Case 3* was also a physician, and speaking of his own attacks, says, "Sometimes they have been brought on by *exposure* to cold and sometimes by other causes, as for example, by a fit of *laughing.*

"All of my earlier attacks came on as far as I can remember, about three o'clock in the morning. They *began* invariably *with* a *cough.* Often when I have been lying flat in bed with my head on the pillow, breathing hard and coughing frequently, I have drawn myself further up in bed, put my arms across the pillow and rested my head on my hand; the coughing has ceased, the breathing has become gradually better, I have slept and waked well." This case related a typical story though not going into great detail.

*Case 4* was a woman 44 years of age who had asthma for 20 years, and quoting from Salter, "She had been accustomed to attribute this first attack to *'cold.'* The expectoration continues, however, for a day or two and indeed may be said never completely to leave; she *spits* a little *every day* and has for years, especially in the morning.'' Here again we find evidence of a chronic respiratory tract infection of long duration, existing even in the free intervals. The morning cough indicates the existence of tuberculosis.

Salter has *Case 5* say, ''My asthma commenced at the early age of three months from a violent attack of *whooping cough* which I had so badly, and which left me in such a suffering and miserable state that it was long before my parents hoped, and still longer, I think, before they expected that I should live.'' The further details were not significant but it should be remembered severe whooping cough produces a great amount of coughing.

From a study of the record of *Case 6,* I can find no evidence of there having been coughs and ''colds,'' but he says, ''In my attacks, the least *dust,* or *smoke* or smell affected me grievously. Even in the intervals between the fits I was exceedingly sensitive to dust, smoke, or smells. I could not sleep in a room where there was scented soap, or green branches, (with which, in such country houses as ours, the fire places used to be dressed in summer), or even heavy smelling flowers,—the wall flower in particular and the violet.

''As the paroxysm advanced, my *head* became *hotter, fuller and heavier;* the *veins* felt *bursting* full on my neck; my eyes were rose colored sometimes; my feet were icy cold. My hands, too, were sometimes cold but not always.''

Speaking of his ultimate relief from asthma, I quote, ''Not only did asthma totally disappear, but *coughs* and *'colds'* and everything like the smallest derangement of any part of the organs of respiration. I grew strong and active and hardy. My weight increased to ten and a half stones though I was taking violent exercise nearly every day.''

In this last paragraph is mentioned that to which he probably was so accustomed that he had not given thought to it as being of etiologic significance.

In *Case 7,* Salter specifically states, ''There were none of the ordinary causes of asthma—infantile bronchitis, measles, whooping cough, nor of old asthma—chronic bronchitis, or heart diseases nor any evidence of asthmatic tendency or nervous temperament.'' But in a footnote he states the *postmortem examination* revealed a marked degree of emphysema together with thickened and contracted bronchial tubes. These latter findings indicate that bronchial inflammation had existed.

Concerning *Case 8,* Salter says, ''She had always had excellent health and was in perfect health at the time, when having overwalked herself and reclined for an hour or so on a couch near an open window, she apparently caught '*cold*' and was seized in the course of three hours (about nine o'clock before going to bed) with a difficulty of breathing, a sense of constriction at the chest, and headache. The idea entertained was that she had caught 'cold' and that the attack was incipient *bronchitis.* The only remedies applied were putting her feet in warm water, a little mustard to her chest, some warm gruel and being put to bed. Gradually, toward morning the breathing began to get easier; profuse frothy expectoration gave increased relief and she was able to lie down as the day came on.'' It probably is not unfair in this case to assume that some chronic bronchitis had existed.

*Case 9,* he has say, ''When a boy, I was subject to *wheezing* and *shortness of breath,* upon any slight '*cold.*' The paroxysm commences with the usual symptoms of 'cold' together with purging and much evacuation of urine, succeeded by intolerable flatus in the stomach and bowels, frequent *convulsive cough,* constant wheezing, with painful dyspnea, being unable to fill the chest with air; any sudden exertion, speaking above a word or two together or attempting to walk up a hill or upstairs brings on, at these times, suffocation; much frothy tenacious saliva is discharged from the throat with some congealed phlegm from the bronchi, and in the mornings what is expectorated is often streaked with blood and sometimes a little pure *blood* is *coughed up.* The paroxysm runs its course in from three to five days when the flatus subsides and expectoration becomes free and easy, being, instead of frothy tenacious saliva and the jelly or white of egg like substance, common phlegm with a little good looking pus.

''In despair, I resorted to the smoke of the stramonium, more with a view toward experiment than from any hopes of good to be derived from it. The effect, however, was wonderful—even to me almost incredible; the very first time I smoked the irritation and a *constant cough ceased* and the flatus was expelled, and I expectorated from the bronchi pieces of clear congealed phlegm from half an inch to about an inch in length and the thickness of a crow's quill, which enabled me to fill the chest with air." Although apparently not considering the cough of much etiologic value, he does not forget that at the time of the relief of the asthma he was free of a constant cough.

*Case 10,* speaking of the exciting causes of his own asthmatic attacks, says they are *"colds," change of air, a recumbent posture, laughing, coughing, sneezing,* bodily *exercise, hay fever* and what is decidedly remarkable, the proximity of a common domestic *cat.* Several of these causes are secondary to others and cannot be easily distinguished; for instance, I do not know that a recumbent posture, or moderate exercise would ever produce a paroxysm without a present tendency from the effect of "cold" and unfavorable air, etc.

"Besides asthma, a foe ever present or near, I was subject to sore throat, *bronchitis,* swollen glands in the neck, enlarged tonsils, eustachian tube deafness, *headaches,* and habitual wakefulness at night, a variable appetite and an inability to stoop my head low, from a feeling of sickness which it invariably produced; I was debarred from the natural and healthful sports of childhood for I could *neither run nor laugh* heartily without danger of a suffocating paroxysm of temporary asthma.

"In my case the most prominent and frequent of all the exciting causes is what is commonly called *taking 'cold,'* and this acts either directly when the asthma becomes the immediate consequence, or remotely through the intervention of inflammation or congestion of the lungs when the asthma comes on later.

"*Coughing,* though a symptom of the complaint, is also a source of aggravation, and when there is no appearance of asthma, is sufficient to call it into existence. A violent fit of *sneezing* in the summer will produce asthma, otherwise not. I have always suffered from the effects of bodily *exercise,* especially in childhood; but even at my present age I cannot run a considerable distance or jump a child or skip with a skipping rope without the occurrence of some asthma."

Speaking of his headaches during an attack he says, "This headache is never present except in a violent paroxysm with which it subsides, commencing after the difficulty of breathing has existed for some little time. Such headaches do not accompany all violent paroxysms of asthma but are of rare occurrence; still they are so peculiar and *characteristic* as to be entitled to rank among the symptoms of asthma. They are unlike any other *headaches,* unaccompanied by nausea and consist of an acute pain over the brows and in the front part of the head and a feeling of fullness; they are greatly aggravated by coughing, during which the pain becomes intense.''

This patient was subject also to both *hay* and *''cat'' asthma* and of these he says, ''But the most conspicuous symptom is the asthma, which most always continues longer than the *sneezing,* since sneezing on such occasions always produces it, and when it has reached the worst it takes some time to subside. The asthma may recur on lying down in bed and disturb the early sleep, but this with me is not of common occurrence.'' This patient told the story about the importance of coughing and sneezing in such plain words that there is no mistaking it.

Salter says of *Case 11,* ''He was quite well up to last October when he caught a *severe 'cold'* on his chest with soreness beneath the sternum, *cough,* and *expectoration* but he did not lay up nor did he seek medical advice. Finding in the following January that he was getting worse, he applied to his medical attendant who told him that he had been and was then suffering from *bronchitis.* He experienced, I think, but little benefit from treatment. It was not till February that the *asthma* showed itself.''

Practically all authors admit that the asthmatics have more or less *inflammation* of some part of the respiratory tract. I would have hesitated to describe any of my own cases in the language used by some of Salter's lest I be accused of allowing my prejudice to influence my observations. What more glowing *support of my theory* could be found than these case histories written in support of theories entirely unlike mine. The literature teems with observations which give support to the ''nonpassive expiration theory'' as the cause of asthma.

But writers on asthma refer also to what some choose to call a *pure asthma,* indicating that there is a type of asthma in which there is no demonstrable inflammation of the air passages and no evident cause. I am open to conviction on this point. I am inclined to the opinion that all cases of asthmatic dyspnea have either an inflammatory process or point of irritation that causes coughing, sneezing, or other prolonged forceful expiration, or that there are other lesions which will tend to produce an increased intraalveolar air tension.

Unquestionably there are records of cases where there was found no demonstrable cause of the asthmatic dyspnea. The references to *"pure nervous asthma"* are less frequent in the modern literature, however, than in that of half a century or more ago. Ideas, once accepted, even though never proved, may be handed down from generation to generation and given credence simply because they have in the past been accepted to such an extent. I have never seen cases of asthma in which there were not some very definite abnormalities.

Most modern writers are satisfied to simply refer to *pure uncomplicated asthma* without discussing it. In this connection, the point I wish to make in quoting part of a chapter from the splendid work of Salter is, that there is little or no ground to assume that asthma is a purely nervous disorder.

He says, "The reasons that force upon one's mind the conviction that asthma is essentially a *nervous disease* are very numerous and not less forcible and convincing; but I shall here be able only briefly to indicate them as their fuller consideration would involve too great a space. They are principally derived from the following considerations: (a) the cause of asthma; (b) its remedies; (c) its associated and precursory symptoms; (d) its periodicity; (e) the absence of organic changes; (f) the circumstance that the phenomena of the disease are muscular.

"We see, in the first place, that the causes of asthma are such as affect the nervous system and such as give rise to other diseases acknowledged on all hands to be nervous. Thus, *fatigue* and physical *exhaustion* and sudden or violent mental *emotion* will bring on an attack. I was informed some short time since, by my friend Dr. Theophilus Thompson, of a case in which on two occasions severe asthma was brought on in a gentleman by sudden *fear* from his having, as he imagined, administered an overdose of belladonna to his wife.

"I know the case of an asthmatic boy some years ago, who used constantly to be warned by his parents not to overexcite himself as if he did, he would be sure to have the asthma the next day; and lately I met with another case in which I was told that when the asthmatic was a little boy he found in his disease a convenient immunity from correction; 'or I shall have the asthma;' and so he would. His *fears* were as correct as they were convenient. *Venereal excitement* will bring on asthma; a gentleman once told me that one of the severest attacks he ever had in his life was brought on in this way.

"Moreover, many well known and recognized causes of asthma can only act on the lungs through the intervention of certain parts of the nervous system; thus, *gastric irritation* can produce spasm of the bronchial tubes only through the intervention of the pneumogastric nerve—it is the only connecting link between the two organs, either physiologically or anatomically."

The consigning of a disease to that *scrap heap* of diagnosis known as "*nervous diseases*" is in my opinion a practice not conducive to advancement in medicine.

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# CHAPTER XXII.

## DIAGNOSIS OF ASTHMA.

Most cases of asthma are recognized as such before the physician sees them. But since a physician usually makes his initial call during the time that the asthmatic paroxysm is at its height and since the recognition of the typical attack of asthma is ordinarily not difficult, the *diagnosis* of asthma is *plain* in most instances. The same expiratory dyspnea is produced in no other condition so far as my experience or my search in the literature teaches me. I make exception to a statement by Berkart[1] in which he says a subglottic tumor may produce expiratory dyspnea simulating asthma. An attack of asthma usually comes on gradually. The dyspnea at first is, as a rule, inspiratory as well as expiratory and the attack may be checked before the expiratory dyspnea develops to the extent typical of asthma.

In accordance with my conception of asthma, there are three things which every case will exhibit; namely, *expiratory dyspnea, wheezing* in the medium sized bronchi, and *emphysema.* Without these three things a case cannot definitely be pronounced asthma. The condition might be preasthmatic or the patient might be asthmatic and not suffering from a paroxysm at the time of examination. All three factors may promptly disappear with the cessation of the subjective dyspnea. In most cases the wheezing will remain for a time and in old asthmatics the emphysema is prone to become permanent.

The amount of *expectoration* is likely to depend upon the severity and duration of the attack. The more severe the swelling and inflammation the more likely are the mucous glands to be stimulated into activity. The wheeze is accentuated more on expiration and especially by a forceful and prolonged one. A cough or a sneeze brings the wheeze out the most.

In a patient who has had many attacks, an attack is likely to begin more or less suddenly. When the *paroxysm* is *fully developed,* the patient will usually be found in a sitting or standing posture with his hands braced on his knees, or some other object so as to fix the shoulders. The face will have an anxious expression and a high color and may be somewhat cyanotic and puffed; the veins about the neck and face will be distended and a sensation of fullness of the head may be complained of, particularly during expiration, and more especially when coughing.

For a time before and during the attack, it will commonly be found that the patient is *coughing;* sometimes the coughing is extremely forceful and straining on him. It has been my observation that the fewer the attacks he has had, the more severe and straining are the paroxysms of coughing, whereas in one who has had numerous attacks the coughing may not be so strenuous.

The amount of expectoration ordinarily will be slight at first and may be either watery and frothy or purulent. Later the sputum increases in quantity, becoming viscid and stringy. A careful examination of the sputum commonly will reveal *pellets* of mucus, *casts* of the bronchi, Curschmann *spirals,* Charcot-Leyden *crystals,* eosinophiles and other *cells.*

The presence of one or more of these constituents of the sputum is confirmative evidence of the diagnosis of chronic bronchitis only and suggestive of asthma. The diagnosis of asthma will generally have been unquestionably made long before the sputum is examined. But when in doubt, the *examination of* the *expectoration* should be made even though all the elements ordinarily found are sometimes discovered in other conditions.

On *physical examination* during an attack it will be found that the chest muscles and all those which can be brought into play to assist expiration are tense. The abdominal muscles especially, will be rigid and firm. The costal angle will be narrow during expiration, the sternum high, the intercostal spaces bulging, and the veins of the chest and neck distended.

The percussion note will be tympanitic perhaps even over the cardiac area. The *diaphragm* will be depressed so that the liver dullness may be a rib or two lower than normal. On auscultation, numerous sibilant and sonorous *râles* and other rhonchi will be heard at all points in the chest unless the condition is unilateral or limited. These sounds are more prominent during expiration as a rule and coughing or other very forceful expiration will increase the intensity of the noises. During the intervals between the attacks the râles and other evidences of bronchitis are prone to persist.

I repeat, the asthmatic dyspnea in *mild attacks* may not be of the typical expiratory order. It may be simply a labored inspiration and a labored expiration of moderate intensity which may or may not later become typically asthmatic. Ordinarily the patient is not seen in these mild attacks; but if he is, the history, the presence of the râles, the type of the chest, the emphysema, and the character of the sputum will assist in arriving at the conclusion that the condition is asthma.

*Bronchitis,* acute or chronic, I believe, is a fairly constant factor in asthma, and may produce more or less fever, purulent excretions from the bronchi, coughing, wheezing, etc., before the asthma develops and between the attacks. The bronchitis, however, may be so mild as not to be detected.

The *complications* of asthma and the contributing factors should always be looked for. I refer to enlarged bronchial lymph glands, early pulmonary tuberculosis, polyps of the nose, sinus infections, nasal catarrh, infected tonsils, pyorrhea, alveolar abscesses, appendicitis, colicystitis, nephritis, heart disease, aneurysm, asthmogenic points in the nose and trachea and other factors which directly or indirectly embarrass the respiration or tend to promote a catarrhal condition of the respiratory passages. The nose and throat examination should also be a routine procedure.

The sputum should always be examined for tubercle bacilli and when the chest has cleared up so that it is feasible, an *examination* for tuberculous foci, including the use of the roentgen ray, should be thoroughly made. In cases where chronic suppurative processes are found, it may be well to isolate the organisms with the idea of using autogenous vaccines if relief cannot otherwise be afforded. The same may be said concerning the organisms which may be responsible for the bronchitis.

It should be remembered that lues may affect the lungs and bronchi and be an important contributing factor toward the cause and continuance of the asthma.

In occasional instances it may be necessary to differentiate between *asthmatic and other dyspnea.* One of the most common contributing causes of dyspnea is an inefficiency of the left side of the heart. This regularly occurs in uncompensated mitral disease and also in aortic disease which causes dilatation of the left ventricle and weakening of the mitral flaps. In such events, there is a damming of the blood into the capillaries of the pulmonary circulation.

The dyspnea affects inspiration especially and evidence of *cardiac* dilatation and *murmurs* will usually be found even on superficial examination. The *dyspnea* may be markedly increased by even a slight amount of exercise, whereas, such may not be so pronounced, as a rule, in cases of asthma. Bloody sputum is common in this dyspnea and relatively rare in asthma. Left ventricle inefficiency and asthma may occur concomitantly and, in such an event, the former would predispose to attacks of the latter.

A *dyspnea* resulting *from* an *aneurysm,* enlarged lymph *glands,* mediastinal *tumor, pneumothorax, etc.,* will usually be diagnosed by the fluoroscope and the roentgen ray plates. Then too these dyspneas are not inclined to be typically paroxysmal; and the expiration is not likely to be more affected than is the inspiration. It should be remembered, however, that these conditions may predispose to asthma. They develop gradually and are inclined to persist till the pathologic factor responsible for the same is removed. An aneurysm, if of sufficient dimensions to interfere with breathing, ordinarily will produce pain, dullness, pulse change, tracheal tug, pulsation, brassy cough, etc.

*Pneumothorax* may produce bulging of the intercosal spaces, displacement of the organs of the chest, alteration of the breath sounds, the coin sound, etc. *Pleuritic effusion* will be proved by withdrawal of fluid. *Tumors* of the larynx or trachea will be discovered by laryngoscopic examination.

There not infrequently occurs with *nephritis* a complication—dyspnea—sometimes known as "nephritic asthma." Unless a careful investigation is made, this condition may be considered to be bronchial asthma. In nephritic dyspnea the lung condition ordinarily will be found to be a simple edema of the lungs; and the urine will contain those elements which signify a severe nephritis; however, it must be remembered that any simple dyspnea may actually set up a true asthma. Dieulafoy[2] says that some of the attacks of the dyspnea in nephritis come on suddenly suggesting asthma.

Minervini and Tagliamuro[3] emphasize the fact that a sufferer from bronchial asthma in contradistinction to cardiac, renal and other asthma, arises and goes toward the *open air* and also usually grabs the back of a chair or other object to fix the arms.

Smith[4] says asthma may have confused with it congenital *laryngeal stridor, thymic asthma,* laryngismus stridulus, and retropharyngeal abscesses.

It should be repeated that all these factors tend to make the act of breathing a *subjective act;* bringing on nonpassive expiration and hence to this extent may be responsible for asthmatic dyspnea.

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# CHAPTER XXIII.

## TREATMENT OF ASTHMA.

The *therapeutics* of asthmatic dyspnea resolves itself into *two parts;* namely, that of the *acute attacks,* and that of the *conditions predisposing* to and causing the paroxysms.

A physician usually sees a case for the first time during a paroxysm and ordinarily the suffering is so acute that the one thought is to give prompt relief from the dyspnea. My own experience with the use of *adrenalin* has been *eminently satisfactory.* Up to the last two or three years I had held the opinion that there was more or less danger attached to the use of it. But the preponderance of evidence now goes to prove that the drug is not only harmless but that it rarely fails to relieve the attacks. I have used it for the most part by hypodermatic or intramuscular injection and have had no bad effects. In one instance the adrenalin given hypodermatically evidently was taken up by a vein. The patient experienced marked though temporary discomfort in which clonic contractions of the skeletal muscles, palpitation, dizziness, general fright, etc., were prominent symptoms. The signs of toxicity passed off in twenty minutes or thereabouts but a fear of the drug remained nearly a week.

From a study of the literature it seems that the endobronchial *administration of* the *adrenalin* works even better than does its hypodermatic injection. It has been demonstrated that the nasal, the bronchial and the tracheal mucosas have the ability to absorb adrenalin with great readiness. Therefore the sufferer from asthma may be given an atomizer and an adrenalin solution to be used whenever the attacks show evidence of developing. I have done this in a comparatively small number of instances with fairly satisfactory results.

Since *adrenalin,* however, does *not* have *a* decided tendency to *cure* asthma it may not be best to give the patient an agent which will afford perfect temporary results. Most cases of asthma can be greatly improved by proper treatment in the intervals between the attacks; and hence if the patient is given an adrenalin spray and is relieved thereby, it should at the same time be particularly impressed upon his mind that other treatment is absolutely essential.

The *action of* the *adrenalin* is doubtless not thoroughly understood. It has been repeatedly observed that concomitant with the use of the adrenalin there occurs a *reduction of the redness, swelling, and hyperemia* of the mucosa of the trachea and bronchi, so far as can be seen with the bronchoscope. It has also been claimed that adrenalin has the power of causing a dilatation of the bronchial muscle fibers, though others hold that this is not true. A fuller discussion of the action of adrenalin may be found in the next chapter.

While the *dilatation of* the *bronchioles* may occur and may be of much importance, it is essential that there be some effect of the drug directly or indirectly upon the mucosa of the moderate sized bronchi where greatest obstruction occurs.

It has been for some time my personal opinion that the drug produces its good because of its well known physiological effect; namely, *constricting* the *arterioles* of the systemic circulation. This implies that the arterioles of the bronchi are constricted by it, thereby directly increasing the lumen of the bronchi. The constriction of the systemic arterioles also directly reduces the rate of the flow of the blood from the arteries to the veins, thus tending to reduce the venous pressure. Since the venous blood pressure is an important factor in causing a congestion of blood in the bronchial mucosa, a reduction of the blood pressure of the vena cava is of importance in the treatment of asthma.

I was led to this conclusion originally by my experiments with *strychnin and morphin.* When these drugs were administered independently of each other there was little or no noticeable effect on the asthma. Morphin, it is well known, does ordinarily relieve asthmatic attacks. I think I used insufficient quantity or my results with it would have been more satisfactory.

The addition of the strychnin was of such pronounced and positive benefit that there was no mistaking its having an effect. The principal physiological *action of strychnin* is, according to Cushny,[1] a constriction of the arterioles by virtue of its stimulating effect on the vasomotor center of the cord.

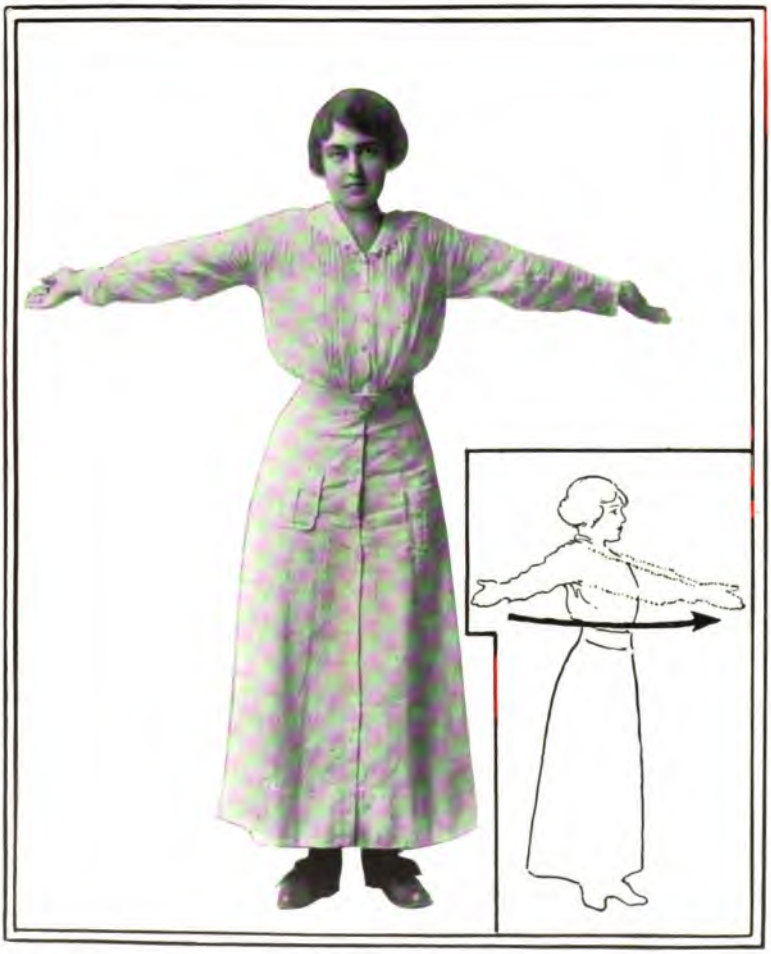

Fig. 35.—Position of Full Inspiration. Respiratory drills are of great importance for

My interpretation of the *good effects of strychnin* was that the constriction of the arterioles of the systemic arterial tree decreased the rapidity with which the blood passed from the large arteries to the veins. This idea was one of the first that evolved from my study of asthma and whether right or wrong, played no small part in leading me to my present conception of the condition.

A constriction of the arterioles of the systemic arterial tree will cause a *rise in* the *blood pressure unless* some other action occurs to compensate for the constriction. In asthma the blood pressure does not, I believe, ordinarily rise with the administration of either the adrenalin or the strychnin and morphin. Although each of these treatments, I hold, causes a constriction of the arterioles, this is compensated for by a slowing of the heart rate and by a reduction of the tonus of the voluntary muscles, both of which result from the sensation of relief the patient has when the attack shows signs of abating.

As much as seven years ago I made the observation, although I did not then understand the explanation thereof, that an attack could be gradually ameliorated by teaching the patient to breathe slowly and deeply, giving proper time to each phase. I now believe the value of the *deliberate* regular *breathing* is that it directly reduces the duration and degree of the increased intra-alveolar pressure during expiration, which in turn, reduces the bronchial swelling. And this, I take it, is one of the decisive arguments in support of my conception of asthma.

By quickening and deepening inspiration and *allowing expiration to take place without muscular effort,* the *tension of the air* in the alveoli comes nearly to that which exists under *normal* conditions.

I recommend that asthmatics be given *respiratory drill* regularly once or twice or even more often daily for 15 to 30 minutes at a time. The method I employ is as follows: the patient stands erect with nothing on the chest or abdomen to interfere with the free movement of the trunk or arms; the arms are extended forward with the palmar surfaces together. With a quick and complete inspiration, the arms and shoulders are thrown backward as far as possible, holding the pectorals taut. This position is held just a second or two and then the arms and shoulders are slowly returned to the starting position, allowing expiration to proceed at the same time, but very slowly and gradually. This attitude is held for a second or two when the cycle is repeated. Theoretically this procedure drains the capillaries of the bronchi by the sharp forceful inspirations; the slow deliberate expiratory movements should do away with the damming of blood and lymph to the bronchial mucosa. It is important to teach the patient that at no time must he allow his expiration to become muscular. He should be taught the dangers from coughing and sneezing and any forceful expirations.

It can be demonstrated that the respiratory *drills* as outlined will temporarily, at least, *do much* toward relieving the conditions which exist in the bronchi of an asthmatic, at least as evidenced by the auscultatory findings. The noises and roughened breathing will often be remarkably improved by a very few minutes of such drill. This method will not remove the inflammation and irritation within the bronchi and hence must be supplemented with other treatment.

The blood from the right side of the heart then flows more readily through the pulmonary capillaries to the pulmonary vein and to the left side of the heart. The pressure in the vena cava is thereby reduced and all tributaries, including the bronchial vein and the bronchial lymph vessels, are drained. This causes a *reduction of the swelling* in the bronchial mucosa which in turn *allows the mucus and detritus* in the bronchi to become loosened and *expectorated.* Thus the bronchi become patent.

It should also be noted that as the respiration becomes deliberate, especially as expiration takes place slowly and without force, the *intraalveolar tension* during expiration *is less,* and consequently proportionately *less is the force applied to the* exterior of the walls of the finest walled *bronchioles;* hence their tendency to be collapsed is relatively decreased.

In *whistling, humming, blowing* mouth harps, etc., it is necessary to inspire deeply and *expire deliberately,* even though muscular effort therein may not be entirely dispensed with. In performing such acts the intrabronchial pressure developed thereby tends to force out the swelling of the mucosa and also to prevent the collapse of the finer tubes. The good effect of this can be demonstrated when the nasal mucosa is congested so that air is admitted with difficulty, if the nostrils are closed by the thumb

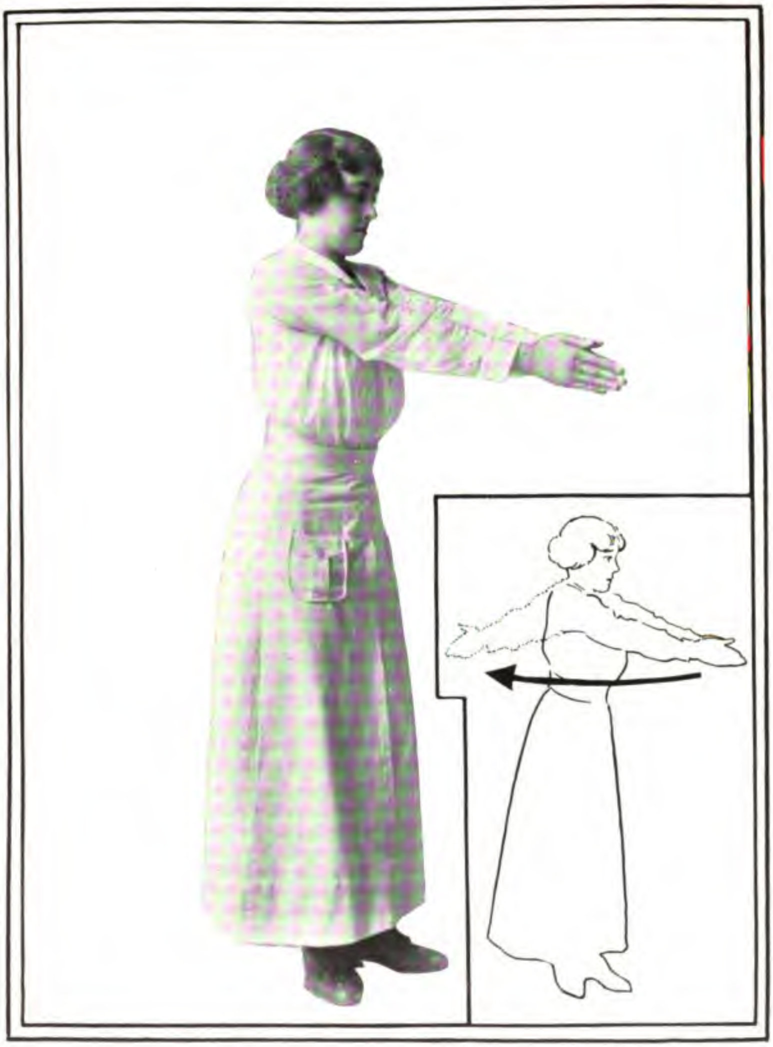

Fig. 36.—Position of Easy Expiration. The expiration must be made slowly, delib-

and finger and the palate is repeatedly contracted in a sort of pumping motion. The hyperemia of the mucosa will be reduced and air will pass more easily through the nose. A similar effect is produced in swollen bronchi by whistling, humming, blowing, etc.

I believe that much of *the good* effect *of* the *smoking* of cigarettes of various ingredients and the inhaling of any of the many commonly recommended drugs may be largely, if not entirely, *due to the slow complete inhalation and the deliberate prolonged expiration,* both of which a sufferer will unwittingly do in order to get the greatest amount of the drugs into the tubes and the longer to hold them there.

From my conception of asthma, after the acute attack is relieved, and after the patient has been taught how to breathe properly, the next most important duty of the physician is to see that his *cough* is properly and promptly *controlled.* The procedure adopted to control the cough will vary perhaps in any two cases.

In one case it may suffice to *teach* the *patient* that *coughing* is a reflex action, a *habit* to be *controlled by* the *will.* In another case, ten to sixty grains of *bromides* may be prescribed with the desired results; or spraying the throat and pharynx with *anesthesin* may dispel the irritation sufficiently. Again it may be necessary to give *intratracheal medication.*

*Inhalations* of the compound tincture of benzoin with creosote, oil of tar, menthol, terebene, etc., in steam from boiling water may be the procedure which will produce the beneficial effects. This, in my experience, has been very satisfactory for most cases. An *opiate* may be required. *Heroin* should, I believe, be the agent of this class to be given preference. The opiates should be used infrequently and in as small dosage as possible and administered only by the physician, nurse, or a member of the family appointed for the task. It should ever be kept in mind that asthma attacks tend to recur again and again; and most asthmatics will not continue any prescribed course of treatment long enough to get permanent relief.

Together with the consideration of coughing should be that of *sneezing.* This comes commonly in the so-called "hay" asthma, "horse" asthma, "cat" asthma or other anaphylactic reactions which affect the nasal mucosa. The sneezing must be controlled just as much as the coughing and some of the measures used against coughing may suffice against the sneezing.

Some years ago I found recommended somewhere for acute coryza an *ointment* composed chiefly *of quinin and vaselin,* as I remember it now. At any rate I have had occasion to make use of such a preparation for coryza of various etiologies. The success resulting from its use has been sufficient to cause me to recommend its trial. *Sprays* of weak solution *of cocaine,* of *adrenalin* and *glycerin* or *anesthesin* with *adrenalin* may be tried when other and less heroic measures fail.

As a next consideration will usually come the condition of the *heart.* Because of the emphysema which regularly exists in asthmatics, it may not be easy to ascertain the degree of cardiac dilatation which may be present. The strain which unavoidably falls upon the right heart is, in my opinion, usually of such a grade in pronounced cases of asthma that treatment of the heart should not be ignored. *Digitalis* usually will be indicated. It will counteract the dilatation of the heart and bring about a better, slower action. Strophanthin, strychnin, camphor, etc., may in certain cases have a peculiar fitness.

It, no doubt, is understood without the saying, that the patient should have prescribed for him a strict course of the *rest cure.* In some cases the course needs to be made very strict indeed. In others a relative rest cure may be required. These "cures" are not satisfactory in the home and are best practiced in a sanatorium.

It is my custom, however, to prescribe strict *rest in bed* under the care of a nurse until all the aggravating symptoms have disappeared and for some time afterward. The severity and tenacity of the symptoms will guide one in deciding about the degree and the duration of the rest cure.

As regards the *diet*—I have not found it necessary to make restrictions in most cases. The patients, however, should be taught to masticate their food thoroughly; copious and definite quantities of liquid should be insisted upon. Due attention to the condition of the alimentary canal should be given in every case.

*Poor elimination* should be *given* most *careful consideration.*

Many individuals fail to drink the amount of water they should even during health, to say nothing about the times when they are ill.

To estimate the amount of *water* which leaves the body daily, with the perspiration, feces, urine, and expired air, is impossible. But the amount will of *necessity* depend upon that taken. Since waste material is eliminated with the water, the more water imbibed the more perfect will be the elimination. This is readily demonstrated in many cases by prescribing two or three glasses of water to be drunk before breakfast each morning. An out of the ordinary free stool will generally result within a short time.

Some years ago I endeavored to demonstrate the *effect* the drinking *of* a large quantity of *water* had on the opsonic index. In the first series of experiments, equal quantities by measure of leucocytes, bacteria emulsion, serum and sodium chloride solutions were mixed. The solutions of sodium chloride varied in concentration from ⅛ to 1/32 mol. A ⅛ mol. solution expressed in decimals is .125 mol. Three parts of a normal concentration to one. part of the mol. 32—.03125 mol. makes a solution of .1015625 mol. In this solution the phagocytes took up twice as many bacteria as in normal solutions. The numbers taken up in the dilutions between .1015625 and .125 mol. bear a relation to the dilution. An increasing of the osmotic tension in a second series using ½ mol. sodium chloride solution making a mixture of .21875 mol. caused the phagocytes to take up 50 per cent less bacteria than when the mixture was isosmotic with the blood. In a third series, my own blood was used, taking samples before, during, and after drinking large quantities of water. The amount of water taken was about four quarts; the time of the experiment was approximately two hours; it was concluded when the amount of urine passed equalled the amount of water imbibed. Samples of blood taken were each mixed with equal parts of bacteria emulsion. The phagocytes of the sample taken while the blood was plethoric with water were slightly less active than was the blood taken before starting the experiment; those of the sample taken at the conclusion of the experiment were 33 1/3 per cent more active.

My first series of experiments show that a *decrease of* the *osmotic tension* of the blood *favors* the action of the phagocytes. The second series indicates that the *elimination of waste* material occasioned by the drinking of a large quantity of water also favors the *action of the phagocytes.* That the samples of blood taken while the blood was plethoric were no more active than that taken before the experiment began is probably due to the dilution, which so reduced the quantity of opsonins in a given quantity of blood as to offset the increased activity of the phagocytes which would occur in blood with a decreased osmotic tension. Then too, elimination of excess water may take place by the skin, kidneys and bowels; and salts and extractions are drawn from the cells so rapidly that perhaps a decrease of the osmotic tension of the blood while in the body is impossible.

These experiments emphasize that the taking of a large quantity of water is of great importance especially for a person with a toxemia. It is well known that in cases with a tendency to uremia, large amounts of water are valuable. There is no gauge of a mild grade of inefficient elimination, hence the only *safe practice* is *to consume* a quantity of *water beyond the actual amount required.* It has been my practice to prescribe for an adult in good health, an average *minimum of four to five pints* of liquid daily.

During disease, the *amount* to be prescribed will depend upon the extent of the toxemia and the amount the patient can be compelled with reasonable persuasion to take. The error will usually be on the side of *too little rather than too much.* A glass each hour on an average, totaling perhaps eight pints in twenty-four hours, is a fair amount and an easy figure to remember and also probably sufficient in the greater number of cases.

When all these things have been attended to, the next step is to decide upon the course of *treatment needed for* the chronic inflammatory condition of the respiratory system. A chronic *bronchitis* may result from or be part of a chronic pulmonary tuberculosis. It is worth repeating that Cabot says chronic bronchitis depends usually upon pulmonary phthisis.

In the absence of other causes of the chronic bronchitis and especially if evidences of pulmonary *tuberculosis* can be found, treatment of this condition should be given. A prolonged *rest* *cure* out of doors is to be insisted upon in those cases that can not be permanently relieved by other measures.

Since the tuberculous processes in these cases are usually, if not always, of a chronic nature, they are frequently to be considered as suitable for the administration of *tuberculin.* This should be given over a long period of time, and the dosage should be increased gradually and cautiously to a high point. Reference may be had to the works of Pottenger[2] and others who have written at length upon the subject of tuberculosis. However, as I consider that a considerable number of asthmatics are subjects for the administration of tuberculin, I may properly give the principles which should guide its use.

It has been said by many writers that *tuberculin is to be used by* an *expert;* justly so, I hold, and to the same extent as the scalpel is to be wielded by an expert. Both are instruments which must be handled delicately or much detriment, rather than good may be produced.

The tuberculin must be considered both as a poison and as a stimulant for the body tissues. According to Vaughan,[3] *tuberculin is* a *protein* and when taken into the body is split. There results from the cleavage, according to this same investigator, a toxic portion and a nontoxic portion. The latter has the property of stimulating the formation of the enzymes, the antibodies, the destroyers of the tuberculin.

Vaughan holds that eventually we will be able to split off from the tuberculin molecule its toxic portion with such exactitude and control that it will be a relatively simple matter to get the *nontoxic portion* in amounts sufficient for therapeutic purposes. From a theoretical standpoint, it seems that it would be of distinct advantage to use this form of tuberculin for the first course of treatment at least. Perhaps, then, it will not be essential to control the dosage with the exactness which we must exercise at present.

As to the *form of tuberculin* to employ, I am not convinced that it makes much difference unless possibly in exceptional cases. I use Koch's old tuberculin or a bacillus emulsion as a rule. I *dilute by taking six small sterile vials.* In each I place 0.9 c.c. of sterile salt solution or sterile water. From the vial of concentrated tuberculin I take with a finely graduated syringe, 0.1 of a c.c. and squirt into vial number one. The contents of number one are thoroughly mixed by the drawing up and the squirting out of the fluid and 0.1 of a c.c. of this is taken and put into vial number two. After mixing this, 0.1 c.c. of number two is put into number three; the same amount of number three into four, four into five, and five into six. Into each vial is then put a drop of phenol or tricresol.

If larger amounts can be used in about three weeks, they should be made up as it is *easier to be exact in using larger quantities.* With a little practice it is not difficult to become so adept that the dilutions one makes will be perhaps not exact, but so nearly so that the personal equation and coefficient of error will be fairly constant and varying generally in the same direction.

My chief *objection to the diluted tuberculins on the market* is that the user of the vaccine knows nothing of the care or lack of care exercised in making them. One might argue that they are probably made in very large quantities and that the coefficient of error is proportionately reduced, but all of this is circumstantial evidence only. Then too, high dilutions in solution are said not to have good keeping qualities. While these objections may not be valid, there is no argument against a careful physician making his own dilutions, as it requires but little time. While the matter of expense is of small concern, the difference is in favor of the home made preparations.

The rubber caps which come with some of the bacterin syringes make very good *caps for the vials;* the needle can be introduced into the bottle through the rubber covered with tricresol. Another little trick of practical value consists in binding the vials together by a strip of adhesive, which will also serve as a label. All of this should be done before making the dilutions.

The more violent von Pirquet reaction the patient gives, the more careful I am to *begin with the smallest doses, increasing very slowly.* Each c.c. of the vials contain .1, .01, .001, .0001, .00001, 000001 c.c. respectively of the original tuberculin. The *first dose* should be, as a rule, .01 to .02 c.c. of dilution number six—an equivalent of .00001 to .00002 mg. of tuberculin. Perhaps the second injection will consist of .04 c.c. of number six and as long as no signs of a reaction occur, the successive doses are gradually increased. A *dose may be given once or twice a week.*

When .12 to .15 c.c. of number six has been administered, the next treatment should be given from dilution number five, beginning with .01 to .02 c.c. and increasing the successive doses slowly as with the previous dilution. By this method of procedure, one is not likely to produce a reaction, and in the event that a reaction is caused, it will surely be a light one.

When the point is reached where more than mild local *reactions* result, I deem it advisable to drop back to a dilution well below what will produce the reactions and to administer a number of injections of this dilution. With one case it may not occur before dilution one to two is reached or perchance until the pure tuberculin is given. Reactions when they occur ordinarily consist of slight redness and induration at the site of injection. With care, the systemic reaction of chill, fever and exacerbation of cough will rarely result, at least not until the largest doses are reached. I make it a fairly consistent practice, after dilutions four and above have been reached, to go back at frequent intervals and give smaller doses, working up slowly each time.

In patients who react but slightly to von Pirquet's test, the *dosage* may be *increased* more rapidly, until the more concentrated dilutions are reached, when the same care should again be exercised. These directions may not be sufficiently specific but let it be emphasized, the dosage should be relatively small and in accordance with the physiologic effect rather than with some user's beautiful dosimetric system. With experience one will develop a system of his own.

In the event that the inflammation of the respiratory tract does not depend entirely or to a sufficient extent upon tuberculosis, another vaccine may be used to advantage. *Stock vaccines* may be tried or an autogenous vaccine* may be made, especially if the former does not prove successful. In most cases it may be advantageous to employ these vaccines before tuberculin is used. In the event that it is deemed advisable to use stock vaccines one should choose a combination of those organisms which are usually found on the mucosa of the respiratory tract. The *autogenous vaccine* is the more scientific agent but it must not be forgotten that this cannot always be readily had. Then too, it may not be easy to obtain cultures of all the organisms responsible for the trouble. So in either case there is a chance of failure.

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*Recently I have used sensitized autogenous vaccines prepared according to the method of W. O. Sweek.

In giving tuberculin or any other vaccine, one should not forget that he is administering poison of which the patient may have already had too much; and one should not introduce a vaccine into the body until it is plainly demonstrated that the disease fighting forces of the body are satisfactorily coping with the poison already in the body. Vaccines are most efficacious as prophylactic agents or as aids in perfecting a cure.

The laryngologist and the dentist should each examine every case. *Any focus of* chronic *infection,* as a sinusitis, tonsillar abscesses, bad teeth, infected gums, etc., should be appropriately and *promptly treated.* The infections of these foci, by direct extension or through the blood or the lymph streams, it should be repeated, may be the cause of the continuance of a chronic general inflammatory process of the respiratory tract. The same should be said of infection anywhere in the body.

In *hay fever asthma* it has been reported by various observers that the use of certain stock or autogenous *vaccines* has been *of* great *service* in relieving the condition. In some instances the results have unquestionably been highly satisfactory. *Hay fever* and other anaphylactic asthmas have also been successfully *treated by immunizing* the subjects *to* the respective *proteins* responsible for the anaphylaxis.

Most if not all cases of asthma should have a *prolonged course of iodide.* This should be administered in small doses for a protracted period the same to be determined by the results. It will rarely be given too long even when continued with short breaks for years. My custom is to add to each ounce of a 100 per cent solution of sodium iodide, two grains of bichloride of mercury and allow five drops or more of the mixture to be taken in water after meals. Some cases will be so benefited by this treatment that they may need little else. These are possibly luetic. All will be more or less benefited by this treatment.

Many explanations of the *action of* the *iodide* in asthma have been given. It is my opinion that the iodide and mercury have a specific effect in reducing capillary sclerosis. This is unquestionably true in syphilis, for one frequently sees tertiary lues with a pronounced pallor and perhaps with more or less cachexia, take on a healthy appearance and a glowing pink color after a few weeks' treatment. It can be shown that the percentage of hemoglobin is not materially affected. The one conclusion then is that more blood is allowed to pass through the capillaries of the skin—and if increased in the skin, will it not be increased in other organs or tissues? If the sclerosis of lues is affected in this way, why not also that of other causes? At any rate, I am sure this has been accomplished in cases that I could not definitely prove to be luetic. Perhaps there occurs also some change which makes possible a more perfect functioning of the vasomotor control, so that vessel dilatation comes more, or possibly constriction less readily. Any treatment that tends to reestablish a vascular tone in the bronchial vessels would be expected to do good. But the iodide and mercury will usually need to be combined with one or more of the other lines of treatment.

Certain patients have a tendency to "catch cold" easily. This is a factor which should be counteracted. The removal of pathologic conditions in the nose, pharynx and adjacent areas may accomplish much, but most cases will usually have to be extremely careful to *avoid exposure,* especially during sudden climatic changes. A *building up* of the general *health* will do much and an even, regular mode of living is always advisable, but when all has been done that can be done a *change of climate* to one more even in temperature may become necessary.

Since asthma is so readily affected by any abnormal condition in almost any part of the body, all abnormalities should be removed. It, however, must be remembered that these remote pathologic conditions are only *predisposing causes;* cure may be effected without their removal and while many cases have apparently been cured by relieving the remote pathology, most cases will not be affected unless attention is also given to the respiratory tract.

When all the various phases of the treatment of asthma have been surveyed, one comes back to a *consideration of* the factor which most of all is responsible for the continuance of *the inflammatory condition of the respiratory passages.* It matters not whether this be dust, smoke, sinusitis, tuberculous foci, infected tonsils, an anaphylactic sensitization to pollen, horse, cat, or egg protein, nasal polyps or other factors alone or in combination, an effort must be made to treat whatever is found to be at fault.

*No two* patients will *receive* exactly the *same treatment* because of the dissimilar predisposing factors in the two cases. *But nevertheless the fundamental principles of respiratory drill, relief for the respiratory tract catarrh, for the anaphylaxis or for other factors causing nonpassive expiration are to be consistently carried out in each case.* The results which I have obtained are encouraging; I have a number of patients who are apparently well; but the number of cases is too small and the time too short for specific claims.

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# CHAPTER XXIV.

## TREATMENT OF ASTHMA (Cont'd)

Knopf,[1] believing that asthma is a neurosis and that asthmatics fail to breathe properly, teaches his patients to respire normally and says this goes far toward effecting a cure. He reported that he had cured five cases of asthma in children by the use of the ordinary dietetic, physical and medicinal measures supplemented with psychic training, systematic *breathing exercises,* and change of environment.

Goldscheider[2] says an asthmatic must learn to control his breathing so as to have normal time for each phase and must also suppress his cough. Treupel[3] writes that the main point is to influence and *control* the *dread of suffocation* and to regulate the breathing. He endeavors to train his patients to breathe regularly and deeply, continuing the exercise for fifteen minutes once or twice daily.

Saenger,[4] in 1909, wrote that five years' experience had only confirmed his belief in the benefits from his method of treating asthma, which consists in training the patient to breathe so as to endure long *pauses between the inspirations.* One way he says is to have him count and then take a short breath, or he can blow or whistle or play on a mouth harmonica instead of counting. Another important point, he says, is to teach the patient to control the tendency to cough as the cough is liable to start the attack of asthma.

Hare[5] calls attention to the "value of common unsophisticated muscular *respiratory drill*" in the cure of asthma. Von Strübing[6] says the most important factor is to teach the patients to regulate their breathing, applying no muscular force to expiration and deepening and slowing inspiration. He also calls attention to the need of treatment for the vasomotor disturbances of the bronchi and for the nervousness.

Hofbauer[7] advises against forced expiration as it is harmful. Einthoven[8] says that if the patient will *breathe* just as *easily* as possible the passing off of the attack will be facilitated. Williams[9] and Chapman[10] each long ago observed that the holding of the breath had a tendency to admit of a few easy expirations.

Berkart[11] also recognized the importance of quiet *tranquil breathing* toward warding off an attack. He says, "The recollection of their past suffering keeps them in a constant state of apprehension. They come to look upon every momentary uneasiness, upon the feeling of an approaching cough, upon the slightest wheezing—all of which would readily subside did they not lose their heads, but breathe quietly—as the signal of a threatening attack which must be nipped in the bud."

Kirchberg[12] trained his patients to inhale sharply and to exhale slowly and completely. He also gave vigorous massage to the chest. Kuhn[13] recommends the use of his respiratory mask on the theory that inspiration and expiration are both prolonged thereby and hence a *normal* type of *respiration* promoted and claims many physicians have found it of value. Siegel[14] recommends bringing the arms forward slowly during expiration and throwing them outward and backward during inspiration, all movements being made slowly and completely.

Stadler[15] advises what he terms *lung gymnastics* in conjunction with adrenalin, atropin, calcium chloride, local treatment of the nose and change of climate. Warschawsky[16] recommends in addition to a warm tub bath, respiration drills which he says are to lessen the time of expiration and to increase the vital capacity.

Zuelzer[17] has devised an *apparatus whereby both inspiration and expiration are facilitated* by a pressure of about 40 cm. of water—a positive pressure in the case of inspiration and a negative pressure at the time of expiration. Pescatore[18] has a machine in combination with a stool so that the *chest* and the abdomen may be both *compressed* rhythmically in order to facilitate expiration. He uses this in the treatment of both emphysema and asthma.

Morison[19] uses a form of *artificial expiration,* pressing with one hand upon the chest and the other upon the upper abdomen of the patient. This he claims gives prompt relief by emptying the chest of air. Pearson[20] says he has found Morison's method very beneficial. Middlemiss[21] and Delius[22] and others have successfully used *hypnosis* in asthma.

Gerber[23] treats his cases by the use of *Berger's apparatus* which is so constructed that while the patient is breathing through a long tube from a container, a suction and pressure apparatus automatically reverses itself so as to apply air massage to the pulmonary mucosa. Various medicines, he says, may be administered through the tube. He claims excellent results for his methods.

Samter[24] recommends for chronic bronchitis and asthma the placing of the patient for a time in a *room with compressed air.* Stewart[25] says that after the acute symptoms have passed the patient should take quite violent *exercise,* enough to cause breathlessness, thus developing pulmonary power. Campbell[26] advises strongly against sudden or excessive exercise and in favor of mild exercises, especially walking.

Brieger and Laquer[27] recommended (1) a firm *binding of the chest* including the shoulders and apices of the lungs, (2) hot compresses to the chest morning and evening for a half hour, and (3) the full bath with water 35° to 40° C. for 15 to 20 minutes. Jackson[28] counsels *out-door sleeping* for all asthmatics. Kohn[29] doubts if operations on the nose are of much avail and speaks strongly in favor of founding sanatoria for the treatment of asthma.

Berkart[11] advises rest—a *rest cure* in all that the words involve—as being the best treatment for asthma. Quoting from him, "It (rest) has indirectly, also a salutary influence upon the nutrition of the bronchial mucous membrane. It is obvious that no one can go about for weeks and months attending to the business of life with a portion of congenitally small lungs obstructed, without throwing some strain upon the heart. It is equally obvious that frequent and often prolonged attacks of asthma must still more increase the strain. . . . . The advantages which are derived from an open air treatment for consumptives are equally great in asthmatics, a goodly number of whom are actually subject to that complaint."

Marcuse[30] pours a gallon or more of cold *water on* the back of the *neck* of the asthmatic two or three times a day from a height of two feet. In his opinion, this tends to relieve nasal congestion which he presupposes causes the attacks.

Günzel[31] applies the *high frequency current* up to 1400 per minute to such nerves as the vagus, spinal accessory, phrenics, sympathetic, etc. The positive electrode is applied to the neck or introduced into the nose. He claims that freer respiration and better ventilation of the lungs is thereby accomplished. Courtade[32] employs the *galvanic current* as a sedative for the pneumogastric nerve.

Schilling,[33] Gottschalk,[34] Rosenfeld[35] Schickler,[36] Immelmann,[37] Eckstein[38] and Zabel[39] have each made use of the *roentgen ray* with good results. Brauer[40] and Klieneberger,[41] however, opposed its use in this condition. There is no uniformity of opinion as to why it is beneficial. Some hold it reduces enlarged bronchial glands and others think it simply improves the bronchitis. Immelmann declared that the x-ray produces favorable results because it liquefies the tenacious mucus of the air passages. Von Strümpell,[42] Tobias,[43] and others have obtained beneficial results from the use of *electric light baths.*

Nicolas[44] has had experiences which lead him to the conclusion that the *sea trip* is to be highly recommended for asthmatics, especially for those whose home surroundings are unhygienic. Widmer[45] advises those afflicted with nervous asthma to go to the *mountains.* Bell[46] says Arizona is free from wind, dust, and sudden *changes of* temperature and hence is a good place for asthmatics. Lamont[47] recommends the *climate* of Colorado as being of great value. Hartog[48] reports that cases were entirely relieved during stays in the North Sea. Edel[49] agrees and says a winter sojourn there is very helpful. Von Planta[50] took 16 children with asthma to the mountains of Switzerland as a last resort and they had no further attacks. Cautley[51] says a high altitude and dry air is suitable for the spasmodic condition, a warm dry climate or seaside air for the catarrh; he thinks high altitudes, however, are contraindicated for emphysema.

Fischer[52] reported on cases which had been treated at the Hydrotherapeutic Institute of Berlin. In general the treatment consisted of hot packs to the chest, hot hand, foot, and general *baths* with cold spray to the abdomen. The cases were commonly improved by these therapeutic measures.

Cohn-Kindborg[53] directed *hot air to the chest* of bronchitics and asthmatics and found that an improvement of the symptoms resulted. They argued that in place of hyperemia resulting, there was actual blood depletion of the lungs. The air was applied at a temperature of 65° to 80° C. Many others have made use of hot baths in one manner or another. Siegel[54] recommends and claims much benefit from the vibration *massage* of two points just below and toward the spine from the lower ends of the scapulæ.

Pirie[55] treated 15 cases of bronchial asthma with *autogenous vaccines* made from the organisms obtained from sputa. Six cases were under treatment a short time only. Of the remaining nine, two were cured, five much improved, one slightly improved, and one unimproved. Klenk[56] writes of the use of autogenous vaccines on four cases, three of whom were relieved. The fourth discontinued treatment on her own volition.

Babcock[57] reports the curing of asthma with *autogenous vaccines* made from the bacteria found in the bronchitic exudate. Jones,[58] Berkart,[11] and others have also obtained relief in some cases by the administration of autogenous vaccines. In most cases the organisms used were from the bronchial sputum, but one worker took the bacteria from the middle turbinates. This author reports that out of 13 cases treated, eight were cured and five markedly improved. Numerous reports may be found, particularly in the journals of proprietary drug houses, of the successful use of the *stock vaccines*. Patton[59] administered 75 c.c. phylacogen subcutaneously in 12 injections, and 27 c.c. intravenously in 14 injections to a case of asthma, and effected a cure.

Boucheron[60] treated one case most efficaciously with *antistreptococcic serum*. Talbot[61] cured six cases of asthma from egg anaphylaxis by the administration of *albumen* beginning with small doses in capsules and gradually increasing the amount. Goodale[62] reports the cure of one case of "horse" asthma by spraying into the pharynx a diluted *horse serum* gradually decreasing the dilution each time.

Maurel[63] treats "hay" asthma by removing whatever pathologic findings there are in the nose and then administering *pollantin*. Billard and Maltet[64] and Lübbert[65] reported the successful use of Dunbar's serum for "hay" asthma. Reuter[66] used diphtheria *antitoxin* in 60 cases of asthma, and 41 of them were cured. It was used by Smith[67] on several cases, 60 per cent of whom were cured; by Gillespie[68] on two cases with good results; and by Pierce[69] in 12 cases with fair results. MacKenzie[70] thinks the antitoxin does good in asthma because of its soothing effects on the mucosa.

Kitzmiller[71] treated himself with an injection of diphtheria antitoxin and five hours later he developed the anaphylactic reaction but for three months he had no attacks. Boone,[72] Willis,[73] and Wiley[74] report fatal results from the use of diphtheria antitoxin in asthma. Wiley's case had apparently had "horse" asthma as he could never be about horses without it.

Gillette[75] administered 2000 units of diphtheria antitoxin to himself for asthma and was completely cured. The same treatment given by him to a patient for the same trouble resulted fatally. Gillette collected statistics upon the action of diphtheria antitoxin upon asthmatics. These were given in a previous chapter. Sanders[76] and Revilliod[77] treated asthmatics with diphtheria antitoxin and the results reported by them were good. However, it is now generally conceded that the administration of diphtheria antitoxin is a practice which may result fatally because of previous sensitization to horse serum. Seemingly nonasthmatics, as well as asthmatics, may belong to this class.

Solis-Cohen,[78] in 1900, first used *adrenal extracts* in the treatment of that type of asthma which he designated due to vasomotor ataxia. Bartlett,[79] in 1901, advised the use of two grains of the desiccated adrenal gland three times daily for asthma; and Kaplin and Bullowe,[80] in 1904, called attention to the value of adrenalin for the same disease. Nowotny,[81] in 1907, observed that a direct application of it with cocaine to the endobronchial mucosa gave marked relief. Since these observations a great many men have reported upon it in asthma. Kaplin[82] used adrenalin by hypodermic administration for the relief of asthmatic attacks. He also recommended it as a prophylactic agent. His results were satisfactory.

Melland[83] uses .25 to 0.5 c.c. of the 1-1000 solution by hypodermic administration. Weijer[84] found that 0.5 c.c. of a 1-1000 solution, when given hypodermatically promptly checked asthmatic attacks. Hertz[85] found that one drop or even half a drop was sufficient in his own paroxysms. Dando[86] said that in his own case no less than five minims of adrenalin were required to check a paroxysm. Hoover and Taylor[87] report a case in which two injections of 15 minims each were required to relieve the attack. Waller[88] has found that adrenalin injections relieve asthma even in successively reduced *dosage*. Meulengracht[89] reports that he has given 1500 injections to one man. The dosage never had to be increased and it always gave relief. Keiper[90] injected into the bronchi five c.c. of a cocaine-adrenalin solution and great relief immediately followed. He reports that two such injections effected an apparent cure. Keyzer[91] prescribed a teaspoonful of a solution of adrenalin—2.5 c.c. of the 1-1000 to 250 c.c. water—to an asthmatic during an attack. The dyspnea was instantly checked.

Meulengracht[89] says that he found it far more effectual for asthmatics than any other remedy. His best *results* were by hypodermic administration. The earlier the injections were given in the attacks, the more satisfactory were the results. Mayer[92] and Blum[93] both give testimony to the great value of adrenalin for acute symptoms. Cloetta[94] found that in experimental asthma adrenalin and atropia worked beautifully in relieving the condition. Jagic[95] reported that he had treated five cases by administering hypodermic injections of adrenalin. The results were good and there were no bad effects.

Ephraim[96] treated 100 cases of asthma by *injecting* cocaine and adrenalin through a rubber catheter *into* the *bronchi;* 72 of the cases were greatly benefited, and 48 of them remained entirely free from attacks for periods varying from 6 to 18 months. He strongly advises the use of adrenalin alone, even by *bronchial spray,* whereby he obtained excellent results. Stephen[97] treated 10 cases by means of a bronchial spray of adrenalin and novocain and his results were very favorable. Burgeois[98] says even in tuberculous asthma, the spray of novocain and adrenalin gave relief and produced no harmful effects. He reports three severe cases of asthma relieved by the intratracheal injection of adrenalin. Kafemann[99] recommends the use of a nasal spray containing Peru balsam, alypin, eumydrin and adrenalin with glycerin and claims excellent results therefrom.

Matthews[100] *sprayed* the 1-1000 solution *into* the *nose* with benefit. He found that it also gave relief when introduced by rectal suppository. Zuelzer[101] used for the chronic catarrh of the bronchi in asthma, inhalations of glycerin and adrenalin. The preparation is called glycirenan. Plesmann[102] recommends adrenalin for the chronic bronchitis. Gerber[23] gives adrenalin and chloretone in aromatic oils in connection with vibratory massage of the bronchi.

Heilskoy and Mahler[103] made 120 endobronchial applications in 30 cases and in no instance were there any toxic effects. Six of the 30 cases were cured, 11 were markedly improved, and 13 received no permanent benefit. Möller[104] found that the *endobronchial method* was *more* lasting and *effective* than any other in reducing redness, swelling and hyperemia. Pick[105] nebulized adrenalin solution for two patients and the results were good. Grünwald[106] sprays a diluted adrenalin solution into the trachea and gets good results. Koessler[107] used it in combination with chloral hydrate successfully. Segel[108] found that in two cases where all other measures failed, a mixture of a one per cent adrenalin solution and oxygen when inhaled gave complete relief.

*Many others* have *used adrenalin* in various combinations with eminent satisfaction. Among these may be mentioned Freudenthal,[109] Clapper,[110] Reilly,[111] Segel[108] Matthews,[100] Galebsky and Tetrap,[112] Galluser,[113] Kraus,[114] Horn,[115] and Large.[116] Galluser and Kraus each obtained excellent results by the direct application of it to the bronchial mucosa. McClanahan[117] found a case in which adrenalin did not give relief so effectually as did morphin.

In regard to the use of *adrenalin,* Berkart[11] quotes Hirsch,[118] Goldschmidt,[119] Falta and Ivcovic,[120] and Gouget,[121] who held it *harmful.* Hirsch refers to a case of sudden death from the use of it. Gouget says even small amounts produce atheroma; and Ivcovic and Falta maintain that it produces glycosuria and degenerative changes.

Weiss[122] obtained splendid results by a combination of *adrenalin and pituitrin.* In 3000 administrations he had no ill effects. Krause[123] reports confirmation of Weiss' work. He thinks pituitrin sensitizes either the respiratory center or the bronchial muscles so as to render adrenalin more effective in relieving asthma. Kepinow[124] came to the same conclusion. Houssay[125] found that the combination of adrenalin and hypophysin was applicable wherever the former alone was, the good effect being prolonged by the pituitrin, and that the reduced dose of the adrenalin did away with its untoward effect. He found that the local action was increased if mixed with pituitrin. The results were not always constant, however.

Schlesinger[126] applied *hypophysis extract endobronchially* in asthma but it was without results unless used with adrenalin. The adrenalin-pituitrin-novocain solution, he says, gave good results. He is conservative, however, about claiming cures therefrom. Purjerz[127] recommends combinations of adrenalin and hypophysis extract for bronchial asthma. Henke,[128] Borchardt,[129] and Krause[130] each reported favorable results from the use of endobronchial spray consisting of adrenalin, pituitrin, and novocain.

Solis-Cohen[131] advises the use of pituitary extracts, especially of the *posterior lobe* and reports good results therefrom in a few cases. Borchardt[132] found that pituitary gland extracts, when injected into asthmatics, lessened the asthma. Crookshank[133] treated 20 patients with pituitary extract, using two grain tablets of the gland night and morning and the results were gratifying although not all cases were cured. Warfel[134] used 10 grains of extract of the *anterior lobe* of the pituitary body on seven cases with highly satisfactory results.

Csepai[135] found that the adrenalin action was not always increased by hypophysis extract.

As regards the *method in which adrenalin produces its* beneficial *results,* there seems to be a difference of opinion. Januschke and Pollak[136] explain the good effect on the ground that it relaxes bronchial spasm. This conclusion they reached in view of the fact that the adrenalin counteracted the experimental asthma resulting from muscarin and from peptone. Its power to produce dilatation of the muscle is, however, not great, they say.

Brodie and Dixon[137] found adrenalin without *effect upon* the bronchiolar *muscle* except when very large doses were used, in which event temporary constriction occurred. Golla and Symes[138] found that in the rabbit and the cat it produced an unmistakable constriction of the bronchioles. On the other hand, Jackson[139] was also able to prove, he thinks, that an injection of it caused a dilatation of the bronchial muscle fibers probably through the pneumogastrics.

Elliot[140] says that the bronchial muscles are absolutely uninfluenced for the reason that muscle tissue unconnected with sympathetic nerve fibers are not influenced by it. In his conclusion he says, "Its single characteristic is its aptness to stimulate plain muscle and gland cells that are or have been in functional union with sympathetic nerve fibers." The muscular *injections* of it, he says, tend to *cause* the *adrenals to discharge* their secretion.

Möller,[104] Ephraim,[141] Heilskoy and Mahler,[103] and others have observed that the direct application of adrenalin causes a *reduction of swelling,* redness, hyperemia, etc., of the mucosa of the trachea and bronchi. Weber[142] found it produced a marked short period contraction of the vessels of the lungs and that this was followed by a brief dilatation, after which there came a period of vessel constriction lasting an hour or more.

Sajous[143] says adrenal extract or the active principle "produces its beneficial effects in two ways: (1) by enabling the blood to take up more oxygen in the lungs and increasing, therefore, tissue oxygenation and (2) by *enhancing the catabolism* of the toxic wastes, toxins, etc., which produce the bronchial spasm."

Nice, Rock, and Courtright[144] conclude from some experimental work that epinephrin *stimulates respiration,* usually in depth and rate, proportional to the effect on blood pressure. Pentimalli[145] found that intravenous injections of large doses of it into rabbits produced a *decrease of the depth and number of respirations* and led finally to a stoppage of respiration. The large doses produced asphyxia within a few minutes. From plethysmographic tracings it was found that it reduced the capacity of the lungs. One c.c. of a one per cent solution into the leg vein of a dog led to a slowing of respiration, but not to a decrease in the depth. Repeated doses did not decrease the rhythm. If the injection were made into a distal branch of the carotid, the number and depth of the respirations were greatly decreased and apnea soon appeared.

Oliver and Schaefer,[146] Langley,[147] Boruttau,[148] Salvioli and Pezzolini,[149] and Kahn[150] say that adrenalin *shortens and slows inspiration while prolonging and slowing expiration.* Fuchs and Roth[151] found in 80 per cent of 20 cases that the subcutaneous injection of one mg. of adrenalin affected the frequency of the *breathing* and that in one half of the cases there was a noticeable *increase in the air respired.* This endured for at least an hour afterward. Januschke and Pollak[136] found that the respiratory *excursion was increased.*

Fühner and Starling[152] say it produced a rise in the pulmonary artery *blood pressure.* Lemann[153] discovered that the injections do not materially affect the blood pressure of asthmatics.

Ephraim[96] made the observation that the *eosinophiles* were greatly reduced following each injection. It should be said, however, that he maintains that further study of these same cases revealed the fact that the eosinophile variation in each case was marked, even without the influence of adrenalin.

Pilcher[154] concludes from his experiments on dogs that the *nasal mucous membrane* is an *excellent place* from which *to get adrenalin absorbed* into the circulation quickly.

Brooks and Kaplin[155] found that animals develop a *tolerance* for adrenalin. They had one rabbit which was immunized so that he could stand 50 drops of the 1-1000 solution. They feel that we need have little fear of the sclerotic changes from therapeutic doses. Gaisböck[156] administered to animals as high as 70 injections of therapeutic doses of adrenalin in less than three months and found that no permanent harm resulted.

Hall's[157] physician *patient took* adrenalin hypodermatically up to *200 ounces,* taking as many as 40 to 60 injections in 24 hours. Without demonstrable cause the physician finally took a turn for the better and became entirely free from the disease. Careful examination of kidneys, arteries, heart, and retinal vessels failed to reveal any sign of a bad effect of the drug. The patient himself reported that three times following the injections he had sudden severe headache, nausea, etc. He recommends that the agent be well diluted in saline and given superficially to avoid striking a vein, which he opines, was the cause of his untoward effects. Harrower[158] has seen one man with asthma who has for many months taken on an average of one ounce of adrenalin per day with only beneficial results.

*Hertz*[85] *describes* the *effect of adrenalin upon himself* in the following language: "I gave myself an injection for the first time during a severe attack of asthma. I used three minims of 1-1000 adrenalin chloride. The result was most remarkable. Within a minute my breathing became easier and less noisy but I felt extremely uncomfortable, my pulse became rapid and my hands tremulous. In five minutes the asthmatic paroxysm was over and my breathing absolutely quiet, but the unpleasant symptoms did not disappear for another 10 or 15 minutes when I fell asleep."

Since this experience he has found that one minim or even half a minim relieves the asthma and produces no uncomfortable effects. He has had only one distressing night in three years and that was when he broke his syringe.

Miller[159] says in regard to the *action of adrenalin* injection that within about one minute there usually follows a period of oppression and perchance faintness with pallor and the pulse increasing to from 110 to 130. These symptoms pass off in five to 10 minutes as a rule. He has seen idiosyncrasies. Two cases showed no effect. Another patient had a rapid irregular pulse for three hours and felt ill for some days. One man stood two injections well, but a third and fourth produced a marked irregularity of his pulse. In a woman, an intravenous administration produced such a marked pallor and faintness as to be alarming. He suggests that adrenalin may have an anaphylactic reaction.

Practically all clinicians recommend the use of sodium or potassium *iodide* for asthmatics. It is by common consent to be given for prolonged periods, usually in small doses. Smith[160] recommends the use of iodine and says that its effect, as well as that of other agents of value in asthma is in reducing swelling of glands or of the respiratory mucosa, thereby removing pressure on asthmogenic points, or in lessening the reflex activity of the pneumogastric. Smith[161] uses the iodine for asthma in children, giving it for a time, then discontinuing and resuming it later, for the best effects.

Bodenstein[162] advises an *organic preparation* of iodine known as iodostarin; Steiner[163] recommends lipoiodine; Nieveling[164] has made use of iodotropin while Tauszk[165] advises sajodin for prolonged periods.

Pal,[166] in a study of *caffein* on experimental asthma found that it caused, through the sympathetic fibers, a dilatation of the bronchi. It counteracted asthma produced by peptone and $\beta$-imidazolylaethylamine and other substances and also caused dilatation of the arterioles of the coronary artery.

Mayer[92] and Blum[93] each says the fact has been generally overlooked that *diuretin* often gives excellent results in asthma. They also advise lime as a prophylactic measure. Blum calls attention to one case that took diuretin for a year and a half without injury and without forming the habit. Goldschmidt[167] recommends for the treatment of the early stage, caffein valerianate 0.25 and theobromin natrium salicylate 0.5 gm. to be made into a powder and one or two taken at the onset of the attack.

Kaufmann[168] as a substitute for a *proprietary remedy* supplied by one Tucker, recommended an inhalant called Tulison and containing Peru balsam 73 per cent, alypin one per cent, eumydrin ½ per cent, adrenalin five per cent of the 1-1000 and glycerin 20 per cent. Avellis[169] gives an extensive list of preparations which have been commonly used as home remedies. Stramonium, potassium nitrate, potassium iodide, and belladonna are the common ingredients of most of them. Brugsch[170] analyzed 23 of the proprietary asthmatic cures commonly found on the market, and discovered potassium iodide and often some narcotic, and a harmless expectorant in most of them. The inhalants generally contained atropin, cocaine, or menthol; and those to smoke had usually some of the solanaceæ with potassium nitrate or nitrite. A list of formulas for powders to burn for asthma was published in the *Journal of the American Medical Association*[171] in the year 1907.

Anders[172] says, "In one of my cases a prolonged paroxysm was cut short by a *calomel* purge followed by an enema." Tivy[173] also finds that ½ to 2 grains of calomel gives great relief for asthma in the acute stages. It seems to benefit the case before purgation. Active purgation with other remedies does not do so well.

Ebstein[174] reports two cases of asthma which were cured by *oil enemas*. One case had a relapse associated with a return of the constipation. This was relieved and likewise the asthma. Broadhurst[175] advises that all asthmatics be given a tablespoon of *paraffin oil* three times daily. He claims marvelous results. Rabagliati[176] recommends the regulation of the *diet*.

Von Terray[177] claims *atropin* as a near specific for asthma on the theory that the disease is a neurosis. Zuelzer[17] recommends atropin because of the fact that experimental asthma produced by the stimulation of the vagi is inhibited by atropin. He uses it hypodermatically. Weiss[178] found that an atropin spray directed at the tonsil and uvula gave splendid relief.

Göppert[179] says that the persistent use of *calcium chloride* leads to considerable improvement. An average dose is four grams daily. In acute attacks he gives one to two grams every two hours. Emmerich and Loew[180] claim for the calcium chloride treatment, plus the effect upon the asthma, an increase in energy, better sleep, a rising of resistance toward infections, a diminution of the tendency to catch cold and a losing of fat by corpulent subjects. Kayser[181] found calcium chloride to be of much prophylactic value. He treated 13 cases with it, and in all but two cases he claims satisfactory results. Hoffmann[182] advises calcium chloride and calcium lactate in combination.

Barnes[183] found the attacks in two cases were relieved by the administration, every two and a half to three hours, of *sodium nitrite* in one grain doses. He thinks it acts specifically on the bronchial muscle, causing its dilatation. Mayer[184] says certain cases giving evidence of a gouty diathesis have their asthma relieved by *treatment for* the *gout*. Nine cases out of forty in his series responded to this treatment. Von Gresic[185] found *aspirin* to be very beneficial in asthma. Even in severe cases it gave excellent results when used in conjunction with morphin. Jepsen[186] says that aspirin ordinarily gave relief. Walb[187] has cured a number of his cases by a prolonged administration of *phosphorus;* he used it where there was evidence of previous rachitis.

The list of empirically used drugs is a long one; only a few can be given here. Campbell[188] uses intratracheal injections of *menthol, glycerin* and *gelatin.* He says the menthol reduces spasm and the gelatin dissolves sputum. Schaefer[189] found that a spray containing a solution of 1.028 per cent *cocaine nitrite* and 0.581 per cent *atropin nitrite* in 32.16 per cent *glycerin* and 66.23 per cent water, if used in the beginning of an asthmatic attack would abort it.

McClanahan[117] uses *oxygen, morphin,* or *chloral* in cases where adrenalin does not act as well as would be expected. Smith[161] recommends potassium iodide, belladonna and ethereal tincture of lobelia at bed time for children with asthma. Campanella[190] in two cases used subcutaneous injections of *methylatropin bromide* and reports good results therefrom.

Goldschmidt,[191] though knowing that many people become addicted to morphin from using it in the attacks, recommends it in very small doses, even for months if necessary. Smith[192] advises giving strychnin for prolonged periods. Moon[193] counsels above all else for asthma in children, small doses of arsenic, especially for prophylaxis.

Large[194] cured one case by endobronchial applications of tincture of iodine and silver nitrate solution. Levi[195] reports that he cured 19 cases by the administration of thyroid extract; Hertoghe[196] also had excellent results from it. Treupel[197] has found electric sweat baths, potassium or sodium iodide, exercise, hydropathy, with a transient change to a more favorable climate, the sea shore or the mountains, to be of importance. Weill[198] discovered that inhalations of carbon dioxide greatly relieved the cough and the dyspnea and cut short the paroxysm.

Empiricism has prevailed to a remarkable extent in the therapeutic procedures directed against asthma even among authorities.

*Dieulafoy*[199] calls attention to the service which may be obtained from the use of datura stramonium, nitrate paper, Espic cigarettes, hypodermic injections of morphia, inhalations of pyridin, bromide of potassium, nitrite of amyl, iodide of codein, iodide of potash, belladonna, arsenic, and cocaine. He says, "I constantly prescribe stramonium smoked in a pipe. The dry leaves should be finely cut up and some small pieces of nitrite paper added." He recommends the continuous use of iodide of potassium in the intervals between the attacks for a long period of time.

*Ingals*[200] calls attention to the value of morphin, chloral, fluid extract of grindelia robusta, nitroglycerin, amyl nitrite, carbon dioxide inhalations, coffee, belladonna, hyoscyamus, potassium bromide, camphor, arsenious acid, potassium nitrite, etc., and says the most effectual method of relieving the acute paroxysm consists in "the administration of morphin and chloral repeated every hour until relief is obtained."

*Anders*[172] calls attention to the fact that among the many agents which have been used are the following; amyl nitrite, coffee, alcohol, fumes of niter-paper, belladonna, hyoscyamus, stramonium, lobelia, tobacco smoke, morphin, atropin, cocaine, strychnin, etc. Quoting from him, "Immediately upon the appearance of the paroxysm, about one pint of strong coffee is to be taken hot (without cream or sugar) and in this way the seizure may sometimes be arrested." He says quick temporary relief may often be obtained by the fumes of niter-paper, which is prepared by pouring a solution of saltpeter over an absorbing paper. The cigarettes are prepared by steeping the leaves to be used—datura stramonium for example—in a concentrated solution of potassium nitrate or chlorate, and after drying, the cigarettes are prepared from these leaves.

*Von Noorden*[201] uses atropin in ascending doses, gr. 1/100 increased gradually to gr. 1/16 daily, after which he gradually diminishes the dosage. He continues this treatment, repeating it every few months, lessening the dose and shortening the course each time. *Osler*[202] calls attention to the value of chloroform, pilocarpin, amyl nitrite, morphin, morphin and strychnin combined, cigarettes of belladonna, henbane, stramonium and lobelia, potassium nitrate, potassium chlorate, oxygen inhalation, potassium iodide, coffee, etc. He says, "The use of compressed air in the pneumatic cabinet is very valuable. . . . . In preventing the recurrence of the attacks there is no remedy so useful as iodide of potassium, which sometimes acts like a specific. From 10 to 20 grains three times a day is usually sufficient. Persistent hydropathy is often of great value." Particular attention, he emphasizes, should be paid to the diet.

*Von Strümpell*[203] says, "Next to potassium iodide, I consider an energetically pursued methodical diaphoretic treatment the most effectual therapy. By the use of the electric light baths, as well as by the other generally employed diaphoretic agents, I have usually obtained good results and occasionally even apparent cures in cases of nervous asthma and of asthmatic bronchiolitis. The patients are placed daily in the electric incandescent light bath, in which they remain from 10 to 15 minutes at the beginning of the treatment and later from 25 to 30 minutes. The incandescent light bath is followed by an ordinary warm bath after which the patient rests for one or two hours. In many cases, after four or five treatments a decided improvement is already observed. The attacks cease, breathing becomes freer, and the respiratory murmur clearer. An apparently complete cure may be attained in three to four weeks."

Von Strümpell also calls attention to the good sometimes attained from nitrite of sodium, nitroglycerin, pyridin, bromide of potassium, belladonna, atropin, amyl nitrite, morphin, chloral, turpentine, chloroform, saltpeter paper fumes, stramonium cigarettes, iodide of ethyl, fluid extract of grindelia robusta, etc. He thinks morphin and chloral are to be used for the very severe attacks with the surest results.

For the flagging heart, *Berkart*[11] would use strong coffee, valerian, camphor, and ammonia, and he says, "In urgent circumstances musk is unquestionably the sovereign remedy." In purely nervous asthma he thinks a few whiffs of chloroform, ether, ethyl chloride, or methylene bichloride may be effective. For the severe attack he advises morphin.

As regards the *approaching attack,* I quote from Berkart: "Rest in bed, sufficient ventilation of the room, and diaphoresis are absolutely indispensable. The cough may be delayed by warm demulcent drinks, by applications of anesthesin to the pharynx, or if need be, by small doses of Dover's powder ~~with~~ or without small doses of camphor and quinin. With this treatment, taken in time, the dyspnea will hardly ever reach such a degree as to require a narcotic."

In regard to a *specific case* he writes: "He was deeply cyanotic, his respiration was very labored and accompanied by loud wheezing. On examining him, it was found that the wheezing was loudest over the vertebra prominens and was thence conducted all over the thorax. I encouraged him to *breathe quietly and deliberately* and gave him a few sips of hot water. In a minute or so he expectorated a tiny pellet of mucus, with the result that all subjective and objective signs disappeared. Air passed freely in and out of his chest and the attack was over. There can be no doubt that here the mucus stuck in the glottis, which it obstructed and where it was thrown into sonorous vibration by the respiratory current; while the fear of an impending suffocation perverted the normal respiration just as the fear of drowning does in a nonswimmer who gets into the water apparently beyond his depth. There can also be no doubt that all nostrums for asthma owe their repute to analogous conditions."

Berkart considers it essential that the asthmatic be taught to keep the *mucous membrane* of the nose and pharynx *free from mucus,* using physiological saline with a small quantity of bichloride of mercury as a nasal douche. In regard to the *diet,* he thinks that the patients should usually be fed small amounts at frequent intervals, the smallest amount being given in the evening. The few patients who are obese should be fed sparingly and those much under weight liberally. He recommends diaphoresis, through the use of warm *baths* at a temperature of 90° to 100° F. with a duration of 10 minutes at first increased gradually to 30 minutes.

He advises strongly against patent medicines and against cocaine, stramonium, and similar drugs. He says in the cases addicted to the use of the various narcotics, the warm bath treatment is especially efficacious and satisfying. He advises against potassium iodide because of the danger of the precipitation of an attack through its influence. Sodium iodide, however, he says is free from this objection. Ammonia chloride, iodopin, tartar emetic, weak infusion of ipecacuanha, apomorphin, sulphate of zinc or copper, ammonia carbonate with camphor and digitalis, he holds, may be of benefit by assisting in the removal of the secretions from the respiratory tract. He recommends the employment of diphtheria antitoxin because of "its solvent action upon the fibrinous exudations."

*Martin*[204] recommends as a palliative treatment, the placing of the patient in bed or in an armchair in a room with the windows open; three grains of calomel and soda; the burning of lobelia stramonium and potassium nitrate in the room; hot compresses to the back and chest; and alternating hot and cold foot and hand baths. These "measures," he says will usually quiet the breathing, but morphin and atropin may need to be used. The diet is limited to orange and lemonade for the first 24 hours. He next recommends the use of potassium iodide to be continued three times a day at least for three months and after this at bed time for two years. He gives carefully prepared rules for the regulation of the diet and says any nasal complication should be righted. Massage of the chest is strongly recommended. He also calls attention to the importance of having the patient strive for a "well regulated expiration" and for deep breathing.

*Hofbauer*[205] says in regard to the treatment of bronchial asthma that training the patients to breathe—emphasizing expiration—has a decided effect in reducing the irritation of the vagus. He calls attention to Loewy's finding that the irritability of the vagus is dependent upon the amount of expansion of the lungs. He again testifies to the value of his "Humm Therapie"—"humming" therapy—which he has applied for eight years and thinks should be used with the respiratory drills. He admits the value of adrenalin and says it has no effect on the bronchial muscle of normal man. He recommends calcium chloride because it lessens the irritable state of the central nervous system.

*Lord*[206] says, "There is no specific treatment. Further study of anaphylaxis in animals may lead to more successful therapy. In the majority of cases, the disease appears to run its course but little influenced by the numerous measures suggested for its relief. New methods apparently successful in isolated or small groups of cases have repeatedly found a place in the literature only to be replaced by other and still newer measures. A drug which appears at one time to have afforded relief, may entirely fail at the next trial in the same or another patient. The more distressing features of the paroxysms can often be alleviated. They may recur at longer intervals or even stop, but it is difficult to estimate the influence of treatment in so variable a disease." He then proceeds to give the list of remedies usually found in text books.

Following out a suggestion of Berkart, Hirschberg,[207] in an asthmatic child with a small chest, *resected* two and three-fifth inches of the *fifth and sixth ribs* on the right side leaving the periosteum. Later he made a false joint at the sternal attachment of the first and second ribs. The results were fairly satisfactory. Altschüler[208] also resected ribs in asthmatics with good results.

Lenormant[209] and Tuffier[210] have each performed *chondrectomy.* The former reports good results in one case and the latter says the good results were only temporary. Andrews[211] recommends the same operation for the fixed chest of old asthmatics and emphysemics in order to give greater ventilation. Goodman[212] reports a case of asthma that was greatly relieved by chondrectomy. In some of the cases, he says, relief seemed to be permanent.

Simply to show how ***nonsensical*** and irrational, yet apparently effective, are some of the *therapeutic agents* recommended and used in asthma, I give the following: Short[213] reports after all ordinary measures had failed, the sister of the patient went to a cemetery and obtained a decaying skull. Some of the bones, well dried and bleached, were pulverized and put in water. A teaspoon of the preparation was given thrice daily. After a short time the asthma disappeared and had not returned after two and a half years. Short offers no explanation.

A great many more references from the literature in regard to the treatment might be given. There seem to be as *many methods* of treating asthma as there are writers on the subject.

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lutely necessary for the physician to give assistance by the use of drugs.

It is surprising, however, to know how often the patient will be able to *control* the *cough* when the proper explanations are made to him. I have found that a narrow, thin elastic band tied snugly about the neck will not infrequently be of great service in causing the desire to cough to subside. Whether the action of the band is of value merely through the suggestion that results from its presence or whether the pressure causes a passive congestion of blood in the larynx and trachea and in this way assists, I do not know. But it has been my opinion that probably each factor played a part and perhaps not the less important one of the two was the hyperemia. The laity are rapidly learning that "*colds*" which tend to be unduly prolonged are factors *predisposing to tuberculosis.* This will also do much to prevent the development of asthma because it means that persons with "colds" that fail to get well promptly will seek the advice of physicians and will not be satisfied until cured.

Deformities and pathologic conditions of the *nose, throat, and mouth* are beginning to *receive* more *attention* than they formerly did, and this will tend to reduce the amount of asthma. *Hay fever* and other anaphylactic conditions are now being *given* appropriate *treatment,* thus reducing the frequency of asthma.

*Individuals with* the distinctive physique designated as the *habitus phthisicus,* when seen by physicians *should be advised* to follow those vocations which offer the least chance of injury to the pulmonary structures and which afford the best chance to *build up their resistance.* It is my practice—and one which I recommend—to use tuberculin on individuals who are under weight, subject to frequent "colds" or otherwise below par in health, especially if no other positive cause than tuberculosis can be ascertained. This should, however, always be done with the full knowledge of the patient.

Sooner or later there will be a campaign inaugurated against *nervousness* and the causes thereof, as there has been against tuberculosis and cancer. This is another factor which will tend to reduce the likelihood of asthma.

Again, at some future time it will be considered of sufficient importance to educate people on the question of *undue physical* *exertion*. Certain of the athletic exercises, as the 440 yard dash and longer races, football, etc., I believe, may produce more or less definite injury to the heart of a participant. When these and other causes of heart strain are eliminated, another of the factors which predispose to asthma will have been checked.

Persons with syphilis or with an undue grade of *capillary*, venous, or arterial *sclerosis* should have treatment for the same, even before symptoms arise therefrom.

Attention to the conditions above mentioned will tend to decrease, not only asthma, but many other chronic conditions, and doubtless some acute ones as well.

# CHAPTER XXVI.

## PROBLEMS BEARING ON ASTHMA.

Taking the position that the theory and facts as I have presented them are approximately correct and established, *many problems* of importance in connection with asthma still remain *unsolved.* Some of these are of such significance as to deserve special discussion.

A distinct case of bronchitis is ordinarily not difficult of recognition. But a *mildly inflammatory state of the bronchi* is more *baffling,* cough not infrequently being about the only symptom. The usual accompanying trachitis or pharyngitis or both will also give the same symptom. The respiratory sounds may exhibit a roughness or a cogwheel character or even fleeting râles. But the râles and even the roughness and cogwheel sounds may be removed by coughing so that at the time of the physician's examination there may be no objective evidence of the inflammation. The mucus and pus may be generally distributed throughout the bronchi and may adhere snugly to the bronchial walls and thus give no evidence of their presence. The cough may be so slight as to pass unnoticed until the mildly inflamed areas are invaded by other and more virulent bacteria.

There are *three* distinct and important *problems* connected *with bronchitis* and asthma. The *first* is to discover some means whereby a *mild bronchitis* can be readily *recognized.* The bronchoscope may be of service in the hands of one skilled in its use; few, however, can qualify for this. A *second* has to do with the chemistry and physics and means to facilitate *the expectoration of* the *extremely viscid sputum* which is often found in asthma. *A third* is one of *therapy.* This becomes especially difficult and important as the process in the bronchi surpasses in activity the original focus or foci of infection, in tonsils, gums, lungs, nose, or other areas.

*Anaphylaxis* brings on sudden swelling of the mucosa of the respiratory tract producing in a short time conditions which bronchitis creates only when of long duration. There are many weighty questions connected with anaphylaxis, not the least of which are its *diagnosis and treatment.* Discovery of the protein responsible for the reaction can at present be only indefinitely accomplished.

The *problems* in connection *with the ubiquitous tubercle bacilli* are ever before us. They have been discussed frequently in recent years and much has been done toward their solution. In relation to asthma and the prophylaxis and treatment thereof, it is important to recognize what may be called the pretuberculous stage; that period (1) when the tubercle bacilli have not produced manifest lesions, (2) when the protective forces of the body are still paramount but slowly waning in power, (3) when the tissues of the host are being changed into suitable soil for the tubercle bacilli, and (4) when the tubercle bacilli are preparing soil for the growth of other invading organisms. Too often these individuals fight the fight alone, and not the least difficult part of the problem is to teach the laity the signs of an incipient decline in health. Physicians must learn that a *diagnosis of "overwork," "run down," "neurasthenia," etc., is not sufficient.*

As to *therapy,* it is also *inadequate to give only "tonics," advice to take a vacation, and temporary care.* Such measures are important; but keeping the individual under constant supervision is yet more imperative. The administration of tuberculin even without positive indications, I believe to be of supreme value; but many other problems as to habits and conditions of work, recreation, dissipation, dress, climate, etc., some of which will be discussed in subsequent paragraphs, must be considered and perhaps in many instances radically changed.

Cases of asthma have been reported in which *syphilis* played such a predominant part that treatment for syphilis relieved the asthma. But I am of the opinion that syphilis exerts an influence, just as positive as in the instances alluded to, though far more subtle, on a large number of cases of asthma—and also it might be added, on many of the victims of numerous other chronic diseases. My suspicion is that the organisms of syphilis may yet be proved to rival those of tuberculosis in dissemination. My contention can be supported by the modern medical literature on the subject, but this is afield from my purpose.

*The facts* seem to be as follows: (1) It has long been recognized that no less than three to five years of treatment are necessary to cure syphilis. (2) Does it seem reasonable, when this amount of time is admittedly necessary, that the disease is likely commonly cured by any treatment? (3) The evidence is beginning to accumulate at any rate, that cures are probably the exception, even with salvarsan, rather than the rule. (4) Careful examinations, especially with the aid of the Wassermann reaction, have shown that practically all "women of the street" are syphilitic. (5) Notorious are the statements of those who are in a position to know, that 90 to 95 per cent or more of all men live or have lived illicit sexual lives. (6) The acquisition of syphilis is not always evidenced by the typical initial lesion; in fact it is proved that there may be no lesion—at least none detectable in some undoubted syphilitics. (7) Many cases of the disease show no recognizable manifestation thereof for years, perhaps for a lifetime, and if signs appear, they often may be so atypical as to escape suspicion. (8) A husband being syphilitic, the wife is all but sure to be. (9) If the organisms are in the mother's body, they are certain to invade the fetus. (10) Even if treatment were curative, a small percentage only of even those with manifestations ever have that chance of cure. (11) These statements being true, it seems that the treponema pallidum has a splendid opportunity to be distributed throughout the human race.

Through the *predilection* of the organisms and their toxins *for* the tissues of the *blood vessels,* a fundamental influence is exerted upon cellular nutrition and metabolism. It has long been known that certain areas, as the ascending aorta, are favorite locations for the manifestations of syphilis; but no tissue is exempt from its effects. It seems possible at least that capillary sclerosis, or capillary narrowing from syphilitic or other changes in the nerves, may be responsible for such a reduction in the amount of blood reaching a part or in the amount of nourishment permeating the capillary walls that the protoplasm thereby affected may undergo serious change so as to be unable to prevent invasion by microbes.

These *changes,* in the greatest number of instances, may *come* about so gradually and *insidiously* that through an adaptation of the tissues for the organisms or toxins, or for both—and of the organisms and toxins, or both, for the tissues, a sort of livable arrangement results for both the host and enemy. Therefore the strikingly characteristic and recognizable pathology may not develop; for years the condition varies perhaps but slightly from normal; but after a time the organisms, having been tolerated by the tissues, may get the upper hand or new species or varieties of germs may invade the tissues and at once produce positive inflammation.

In one individual the area of *capillary sclerosis* or narrowing may be in the skin, in another in the heart, kidney, ductless glands, brain, lungs, or bronchi, etc., leading to dermatitis, endocarditis, myocarditis, nephritis, a disturbance of internal secretion, insanity or other malfunction of the brain, consumption, or bronchitis, etc., respectively.

And since bronchitis, tuberculosis, heart disease, nephritis, etc., may be *important factors* contributing toward asthma, syphilis and its many ramifying problems become doubly important in connection with this subject.

The question of syphilis is directly dependent upon that of *morals,* and this has baffled the best of the ecclesiastic as well as of the medical minds of all time. I have no solution to offer. I have the firm conviction, however, that every young man, before he sows his "wild oats" should be apprised of the facts. He should know what it may mean to his own health; he should know what it may mean to the wife he hopes or should hope to have; and he should also know what untold misery the irregular life may mean to future generations, not only to his own sons and daughters, but possibly to his grandchildren and even to his great grandchildren.

In addition, there should be stimulated in young men the *"gentleman sportsman's"* desire to *play fair,*—the spirit of the soldier, Spartan-like, to do right or die,—to be just as resolutely clean as he expects that one he hopes to lead to the marriage altar to be. Economic questions must be so adjusted that early marriages are possible. Far better that the father should plan to support two, his son and the son's legitimate wife, even while the young man is yet in college, than to not only support the son but indirectly and unknowingly partially support one or more women and in the end have his son's health impaired.

But most good will doubtless accrue by *instilling early into the minds of the youths,* especially of the males, *a desire to marry.* This desire coupled with the play fair ideal and backed up with a knowledge of the serious consequences will at least not leave a man in a position to say later in life, "No one took the trouble to explain things to me."

Acute respiratory tract catarrhs commonly designated as "*colds*" deserve more study than they have received to date. It is evident that contagion plays an important role. Perhaps we shall learn to prevent the spread of the infectious material, or we may afford individual protection. Possibly some of the epidemics are borne by the water, milk, or other food stuff. Certain factors, as hypertrophied turbinates, polyps, sinus involvements, diseased tonsils, pyorrhea, tuberculosis, etc., doubtless play an important part in making some individuals more susceptible than the average to "colds."

Whether "*colds*" result *from* the ordinary bacteria commonly found in the nose and pharynx, or whether there are *other agents, as a filterable virus,* which are responsible, we do not know. Possibly anaphylactic reactions to unusual substances of the atmosphere may occur more often than is supposed: possibly simple irritants on a hypersensitive mucous membrane may exert an influence.

Again it may be an *unstable vasomotor system* which allows vasoconstriction of the skin surface to cause a congestion and lowered resistance of mucous surfaces. Certain it is that exposure to unusual drafts renders some persons liable to "colds." It is a congestion? Does the cold have some direct effect on the immunity forces or on the growth of bacteria? Are there changes in the vessels of the mucosa so that a very slight congestion lowers the resistance sufficiently to allow further growth of the ever present microbes?

Why do "*colds*" *predispose to* development of *tuberculosis?* Is it that they are simply a tax on the entire system, the same as occurs with any infection, or is there a more intimate connection? Perhaps the proteins of the germs of ordinary "colds" are closely related to those of the tubercle bacilli, so that a surplus of the toxins of "colds" has a paralyzing effect upon the production of the antibodies for the bacteria of both tuberculosis and "colds." Too much stress will not likely be placed upon this question from the standpoint of asthma.

Since *climatic changes,* especially the sudden ones, *influence tu-*

*berculosis, bronchitis, "colds," nasal catarrh, etc.*, and since no climate is entirely free from some marked changes, it behooves us to know how to *compensate for them.* I think perhaps there has been a tendency with many people to wear during the winter very heavy underwear. Because of this the body is often too warm when in the house, especially if the furnace has been working a trifle too well, and on leaving the house a rapid cooling of the overheated body is caused by a cold winter atmosphere. I think a light weight full length under suit is preferable, but one should have overcoats and other outer apparel appropriate for all temperatures and for all grades of physical exertion. It is the custom also to wear no heavier dress for the feet out of doors than in the house. The regulation overshoe should doubtless come into more general use.

As regards the *outer dress* for the body, I am inclined to the opinion that an improvement in our overcoat might be effected. An overtrousers would likely answer the need. For women, the question is not so simple. Skirts do not protect the legs sufficiently for all occasions. An improvement has resulted in the decrease in the number and width of petticoats. But a woman should use a close fitting covering for the legs to be drawn on under the skirts when going into the cold and to be removed on returning to sufficiently warm quarters.

*Style governs dress too exactly.* How ridiculous and perhaps much in danger is the young woman with heavy furs over the shoulders atop a heavy coat and with the legs from nearly the knees down covered with only thin silk hose and slippers! It is not the filmy party dress which affords insufficient protection for a wait on the street corner after the ball, for the taxi or the street car, but it is the lack of jersey underdrawers, overshoes, and heavy overcoat—all of which should be easily put on and should make an appearance commensurate with the whims of the individual. If Dame Fashion can cause a young woman to wear summer furs and a brilliant red sweater on a sweltering hot summer day, surely she can manage the other.

In direct relation to the question of compensation for climatic changes by means of proper dress are those of *living out of doors* as much as possible and the proper ventilating, heating, and cooling of houses. Some people are in the open to such an extent, and others out so seldom, that exposure is the result in each instance. It is problematical as to how best to temper the condition for both classes, but it should be done. Certainly great good would accrue if houses had screened sleeping porches and it became the habit to use them both winter and summer; in the summer they could be used in the day as well as at night.

This subject leads up to a related and an extremely important problem; namely, that of *recreation*. In this money-mad day but little else than earning power counts. Golfing, automobiling, tennis, baseball, etc., are accomplishing much, but there is a large class of individuals who can scarcely afford these. There is another class who might afford it but who have their noses to the grindstone with no let up till a break in health comes. The play grounds movement in behalf of the children is commendable. Some thought, however, should also be given the play of adults.

*Worry* is a "bugaboo" and probably always will be. But recreation, improved living and working conditions, etc., will have a wonderful influence toward decreasing it.

*Living wages* are also in a measure ephemeral in character because as the income grows, apace grows the desires, at least in a percentage of the cases. This is not an argument against increasing wages; provision should be made for work on public projects nonurgent in character to be had at any time, and at wages slightly less than those paid for similar character of work elsewhere.

In connection with certain occupations there are deleterious *dusts and irritating substances* which should be properly disposed of so as to prevent their being inspired by the laborers. In many instances masks or respirators are provided, and the real problem often is to teach the men the importance of wearing them.

*Alcohol* exerts its effects in many ways. One may become intoxicated from it and submit himself to exposure he otherwise would avoid, and thus be liable to "colds," grip, tuberculosis, etc. Or under its influence, he may submit himself to the dangers of syphilitic infection. Then again, alcohol reduces a man's earning power, causing his family to undergo privations, possibly even starvation, exposure, etc., and indirectly leads to lowered resistance and disease. This problem has such a multitude of ramifications that it is possible to touch but a few of them.

*Water in considerable quantities is essential* for the proper functioning of the body. The water in beverages with a low content of alcohol (for example, beer) if properly consumed may offset the evil effects of the alcohol. Since beer has been such a popular drink, it seems that a de-alcoholized beer would surely do much good. This, it appears, is now being accomplished. Water, however, serves the full purpose of even near-beer if sufficient amount is drunk. Many people drink but a glass or two of water per day. The difficulty lies not only in teaching people that they need *12 to 15 glasses per day* but in teaching them to remember it regularly throughout the day. Two or three glasses of water with each meal are now known to be beneficial.

Variations in *weight* have long been regarded as largely uncontrollable. We are beginning to realize, however, that weight can be controlled; and it is important that it should be. Both under- and overweight are fraught with dire consequences. The former leads especially to tuberculosis, and the latter to cardiac embarrassment perhaps more than to anything else. Appetite, digestion, assimilation, and metabolism may each be variable. The man with none of them good is nearly sure to be thin, and vice versa. Perfection is the result of practice. The man who has always had a poor appetite has not created a demand for perfection in digestion, assimiliation, and metabolism; and, therefore, as these processes have not been stirred to average activity, there has been no call for the appetite to come up to average. Eating, in addition to being a necessity, is a habit; many people have just never acquired the habit of eating enough. Perhaps they have been taught restraint or perhaps their associates always ate lightly. But often the cause has been a "finicky" or erratic conception of what was or was not good for the digestion. Whatever may be the cause of the underweight, sufficient increase of the amount eaten will generally raise the weight. This should be done. Overweight will be reduced by a sufficient reduction in diet. The weight of an individual rather than his appetite should govern the amount he eats.

Just to what extent and how the glands of internal secretion govern weight is not fully known, but that they assist is certain. The *endocrinous glands* indirectly through their effect on weight at least, surely have some influence on an occasional case of asthma; and the fact that various internal secretions have a decided effect on treatment of some cases shows that possibly these glands may not infrequently be connected with asthma, possibly in some more intimate way. They may by vasomotor control, or rather by the lack of it, allow the development of asthma.

*Pyorrhea* predisposes to respiratory tract catarrh, heart infections, kidney diseases, etc., and therefore may predispose to asthma. The cure of pyorrhea is not such an unsettled question as it was a few years ago. But to get people to give attention to the teeth and gums is the problem. With some, not even the esthetic sense causes attention to be given to the mouth in time to ward off serious trouble.

*Heredity* factors are influential in some cases of asthma. Whether these consist of predispositions to bronchitis, arteriocapillary sclerosis, highly irritable nervous systems, or other conditions any of which may play a part in asthma is not known. Possibly certain diseases, as syphilis, are congenital. Or it may be that vascular sclerosis is the fundamental condition and that the tendency to, or the soil for, bronchitis or tuberculosis or irritable nervous system, etc., is a secondary development to the blood vessel changes. The supreme problem is the prevention or prophylaxis of the hereditary weaknesses, but until this is done it is incumbent upon us to recognize the tendencies and to correct or ameliorate them as best we can.

Some there are who claim that *rachitis* is a condition which predisposes to asthma by causing maldevelopment of the nose. While the probabilities are that this exerts only a minor role at most, we should determine accurately about it and be prepared to deal with it if found.

What has been said of rachitis should also be said of *gout;* it seems probable that gout in some indirect way plays a positive role in a considerable number of cases of asthma.

Most asthmatics suffer from *neuroses* or *psychoses* or both. My theory explains, I think, why these disturbances of the nervous system exert such a marked influence. The problem is to teach the patient proper control of his nerves and centers. I think there is no argument but that this should be done by giving the patient a plain statement of such facts as his mental qualifications warrant. The presentation of the truth to any two patients and by any two physicians will vary. The question is an important one for each case and is individual for each physician and with each of his patients.

So much has been said of *vagotonia,* and the argument that a hypertonic condition of the vagi may at least contribute toward asthma seems so conclusive that the problem is either to ascertain how the effects are produced or to disprove the claims which have been made therefor.

*Muscle spasm,* I maintain, does not play more than a contributing part in any case of asthma, and probably exerts an important role but rarely. Whether or not my conceptions are correct is the question. If they are not correct, and it can scarcely be expected that I have hit upon an entirely exact explanation, it must be discovered just how far the muscle may contribute toward the start of asthma, and in what type of cases.

Many other problems are indirectly connected with asthma. But when these have been gone over and over, we come back to the questions of (1) the dilated venules and capillaries of the bronchial *mucosa* and how to overcome them when once produced; (2) the strains of the *right heart* and the nourishment thereof, and how to estimate them; (3) the chronic bronchitis and how to cure it; (4) the methods of preventing *nonpassive expiration;* and (5) the evil effects of coughing and sneezing, and how to educate physicians and patients thereon.

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